April 1991
Volume 36, Number 4
ISSN 00989142-RECACP

RESPIRATORY CARE

A MONTHLY SCIENCE JOURNAL
34TH YEAR—ESTABLISHED 1956

1991 Call for Open Forum Abstracts

- Portable Airway-Suction Systems: A Comparison of Performance
- Fracture of an Intubation Stylet: Case Report
- Chest Physiotherapy in Review
- Twenty-Five Years of Progress in Hyaline Membrane Disease
- Symposium Papers: Long-Term Mechanical Ventilation
  - Physiologic Rationale for Resting the Ventilatory Muscles
  - LTMV as Elective Therapy: Clinical Status and Future Prospects

We've Redefined Value

val•ue (val′yo͞o) *n.* [< *L. valere,* be worth] **1.** the worth of a thing money or goods **2.** estimated worth **3.** purchasing power **4.** th quality of a thing that makes it more or less desirable, useful, et **5.** a thing or quality having intrinsic worth. 6. 5-Year Warranty

Introducing the 7200® Series 5-Year Warranty.

An investment in a 7200 Series ventilator is an investment in value.

The five year warranty… another reason Puritan-Bennett is the smartest investment you can make for your hospital.

Five years… now that's value.

For more information call 1-800-255-6773 or FAX 1-800-755-8075.

We're in it for Life

PB PURITAN BENNETT®

Circle 152 on reader service card

Choose the best filter for your environment.

When you need quality filters for dry inhalation or wet exhalation environments, all you have to do is choose Puritan-Bennett.

Our durable OmniFilter combines dependable filtration and reusable performance in any inhalation or heated exhalation application.

Our low-cost Single-Patient Use (SPU) filter delivers dependable filtration and disposable convenience for your 7200® Series heated exhalation uses.

So for any application, in any environment there's really just one choice to make. Puritan-Bennett filtration products.

Find out more. Call 1-800-255-6773.

We're in it for Life

PB PURITAN BENNETT®

Circle 119 on reader service card

And Now For The Network News.

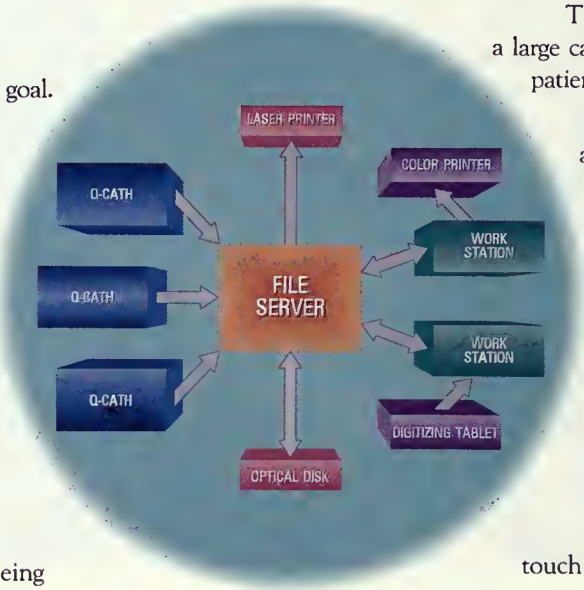
Efficiency.

It's the goal of every cath lab.

Yet, often it's an unattainable goal. Because no matter how advanced your recording and monitoring equipment, it doesn't do you a bit of good if you can't quickly retrieve a patient's data.

That's why more and more doctors and technicians are discovering the advantages a cath lab network has to offer.

They're discovering it's a far more efficient way to operate.



Introducing the Q-cath™ networking option.

All Q-cath systems are now being offered with a local area network option.

That means your cath lab can benefit from improved accessibility of patient data, increased storage space for that data, and a main Q-cath unit that's not tied up performing review and analysis.

How the network works.

The heart of the system is a dedicated, IBM®-compatible, 386-based file server.

It acts as the "hub" of the Q-cath network by handling all centralized data storage. Once data is transferred to the server, it can be accessed by any remote workstation or main Q-cath unit plugged into the network.

All Q-cath units and workstations on the network can also access a shared network tape drive and laser printer.

So what?

So plenty.

Because of the central file server configuration, all data is accessed much more easily.

From many more places.

Analysis of any patient's data can be done from any location (either a workstation or main unit), anywhere on the network.

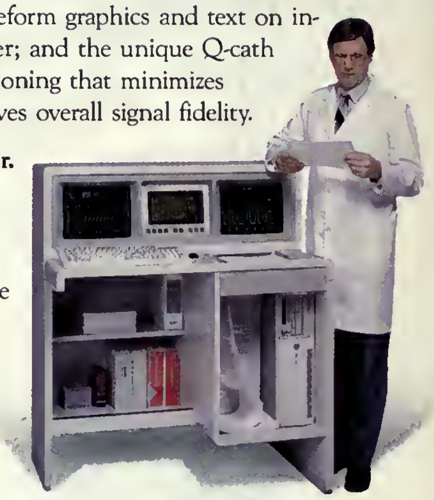
The file server also comes with a large capacity hard disk for storing patient data.

What's more, because review and analysis can be performed at any workstation, the main Q-cath unit remains free to perform more cath lab tests.

The other reasons for picking Q-cath are still there too.

All the features that have built the Q-cath reputation over the years are still included in every Q-cath system.

Features like a convenient touch screen that provides quick, easy access to commonly-used functions; user-programmable procedures that allow you to run an entire case by pressing one button; a high-resolution chart recorder that prints waveform graphics and text on inexpensive, non-fade paper; and the unique Q-cath method of signal conditioning that minimizes baseline drift and improves overall signal fidelity.



You've got our number.

For more on how to take advantage of all that a Q-cath local area network has to offer, give us a call toll free.

2121 Terry Avenue; Seattle, WA 98121-2791
Telex 3794094 QUINTON SEA; FAX 206/223-8465
USA and Canada call toll free:
Domestic Sales **800/426-0347**, Canada Sales **800/633-2888**
INTERNATIONAL SALES
Latin America and Asia-Pacific: Telephone: 206/223-7373, FAX 206/467-8326
Europa/Lode B.V. Groningen, Netherlands Telephone: 31-050-712811, FAX 31-050-716746
Middle East/Dubai, U.A.E. Telephone: 971-4-522285, FAX 971-4-523923

Quinton®
instrument co.

Circle 129 on reader service card

---

* IBM is a registered trademark of International Business Machines.

RESPIRATORY CARE

A Monthly Science Journal. Established 1956. Official Journal of the American Association for Respiratory Care.

EDITORIAL OFFICE
11030 Ables Lane
Dallas TX 75229
(214) 243-2272

EDITOR
Pat Brougher RRT

ASSOCIATE EDITOR
Gary Peck RPFT RRT

ADJUNCT EDITOR
Philip Kittredge RRT

MANAGING EDITOR
Ray Masferrer RRT

EDITORIAL COORDINATOR
Donna Stephens

EDITORIAL BOARD
Neil MacIntyre MD, Chairman
Thomas A Barnes EdD RRT
Richard D Branson RRT
Robert L Chatburn RRT
Charles G Durbin Jr MD
Thomas D East PhD
Dean Hess MEd RRT
Robert M Kacmarek PhD RRT
David J Pierson MD
James K Stoller MD

CONSULTING EDITORS
Frank E Biondo BS RRT
Howard J Birenbaum MD
John G Burford MD
Bob Demers BS RRT
Douglas B Eden BS RRT
Donald R Elton MD
Robert R Fluck Jr MS RRT
Ronald B George MD
James M Hurst MD
Charles G Irvin PhD
MS Jastremski MD
Hugh S Mathewson MD
Michael McPeck BS RRT
Richard R Richard BS RRT
John Shigeoka MD
R Brian Smith MD
Jack Wanger RCPT RRT
Jeffrey J Ward MEd RRT

JOURNAL ASSOCIATES
Stephen M Ayres MD
Reuben M Cherniack MD
Joseph M Civetta MD
John B Downs MD
Donald F Egan MD
Gareth B Gish MS RRT
George Gregory MD
Ake Grenvik MD
H Frederick Helmholz Jr MD
John E Hodgkin MD
William F Miller MD
Ellan J Nelson RN RRT
Thomas L Petty MD
Alan K Pierce MD
Henning Pontoppidan MD
John W Severinghaus MD
Barry A Shapiro MD

PRODUCTION STAFF
Donna Knauf
Jeannie Marchant
Jude Revoli

CONTENTS

April 1991
Volume 36, Number 4

ORIGINAL CONTRIBUTIONS

259 Portable Airway-Suction Systems: A Comparison of Performance
by John F Curran, Kevin S Stanek, and Robert M Kacmarek—Boston, Massachusetts

267 Fracture of an Intubation Stylet: Airway Compromise and Retrieval
by Erick A Kimmerling, James K Smith, and Michael F Tenholder—Augusta, Georgia

REVIEWS, OVERVIEWS, & UPDATES

270 Chest Physiotherapy in Review
by Nemr Eid, John Buchheit, Michelle Neuling, and Harry Phelps—Louisville, Kentucky

DONALD F EGAN SCIENTIFIC LECTURE

283 Twenty-Five Years of Progress in Hyaline Membrane Disease
by Mary Ellen Avery—Boston, Massachusetts

SYMPOSIUM PAPERS

288 Long-Term Mechanical Ventilation as Elective Therapy: An Introduction
by Roger S Goldstein and David J Pierson—Toronto, Canada, and Seattle, Washington

290 Physiologic Rationale for Resting the Ventilatory Muscles
by James K Stoller—Cleveland, Ohio

297 Long-Term Mechanical Ventilation as Elective Therapy: Clinical Status and Future Prospects
by Roger S Goldstein and Monica A Avendano—Toronto, Canada

DRUG CAPSULE

306 Antiviral Agents for Prevention of the Common Cold
by Hugh S Mathewson—Kansas City, Kansas

TEST YOUR RADIOLOGIC SKILL

310 Interstitial Disease with Pleural Effusion
by KI Gourgoulianis, ST Gougoulakis, V Tsakraklides, and C Melissinos—Athens, Greece

BOOKS, FILMS, TAPES, & SOFTWARE

314 Workbook To Accompany Respiratory Therapy Equipment, 4th ed, by Stephen P McPherson RRT
reviewed by Robert R Weilacher—Palestine, Texas

RESPIRATORY CARE (ISSN 00989142) is a monthly publication of Daedalus Enterprises, Inc, for the American Association for Respiratory Care. Copyright © 1991 by Daedalus Enterprises Inc, 11030 Ables Lane, Dallas TX 75229. All rights reserved. Reproduction in whole or in part without the express, written permission of Daedalus Enterprises, Inc, is prohibited. The opinions expressed in any article or editorial are those of the author and do not necessarily reflect the views of Daedalus Enterprises, Inc, the Editorial Board, or the American Association for Respiratory Care. Neither can Daedalus Enterprises, Inc, the Editorial Board, or the American Association for Respiratory Care be responsible for the consequences of the clinical applications of any methods or devices described herein.

RESPIRATORY CARE is indexed in *Hospital Literature Index* and in *Cumulative Index to Nursing* and *Allied Health Literature*.

Subscription Rates: $5.00 per copy; $50.00 per year (12 issues) in the US; $70.00 in all other countries (add $84.00 for air mail).

Second Class Postage paid at Dallas, TX. POSTMASTER: Send address changes to RESPIRATORY CARE, Daedalus Enterprises, Inc, 11030 Ables Lane, Dallas TX 75229.

SleepLab™ Diagnostics... With Home Follow Up

Compatible Systems, Consistent Analysis & Reports

CNS SleepLab™ System

The most widely used computerized sleep system for **adult & pediatric** applications. Computer aided and automated analysis programs include: Staging, Apnea, CPAP, Oximetry, Arrhythmia, PLMS, Sleep Fragmentation, MSLT, pH and more.

CNS SleepLab Systems (1 or 2 bed) can be configured to have built-in amplifiers or to interface to the lab's existing polygraphs. The CNS SleepLab is a turn-key system designed with advanced technology.

CNS Poly G™ System

Poly G is a portable apnea recording system for CPAP/post surgical followup of sleep apnea patients, recording ICU patients and neonatal testing in the hospital, the sleep lab, or the home. Computerized analysis requires **IBM**, **IBM compatible** or **CNS SleepLab Systems**.

CNS®

CNS, Inc., 1250 Park Road • Chanhassen, Minnesota 55317-9260
(800) 843-2978, in MN (612) 474-7600

IBM is a registered trademark of International Business Machines Corp.
CNS is a registered trademark of CNS, Inc.. Sleeplab is a trademark of CNS, Inc.. Poly G is a trademark of CNS, Inc..

Circle 134 on reader service card

MANUSCRIPT SUBMISSION

Instructions for Authors and Typists is printed near the end of every issue of RESPIRATORY CARE.

PHOTOCOPYING & QUOTATION

PHOTOCOPYING. Any material in this journal that is copyrighted by Daedalus Enterprises, Inc. may be photocopied for noncommercial purposes of scientific or educational advancement.

QUOTATION. Anyone may, without permission, quote up to 500 words of material in this journal that is copyrighted by Daedalus Enterprises, Inc., provided the quotation is for noncommercial use, and provided RESPIRATORY CARE is credited. Longer quotation requires written approval by the author and publisher.

SUBSCRIPTIONS/CHANGE OF ADDRESS

RESPIRATORY CARE
11030 Ables Lane
Dallas TX 75229
(214) 243-2272

SUBSCRIPTIONS. Individual subscription rates are $50.00 per year (12 issues) in the U.S. and Puerto Rico, $70.00 per year in all other countries; $95.00 for 2 years in the U.S. and Puerto Rico, $135.00 in all other countries; and $140.00 for 3 years in the U.S. and Puerto Rico, $200.00 in all other countries (add $84.00 per year for air mail). Annual organizational subscriptions are offered to members of associations according to their membership enrollment as follows: 101-500 members—$5.00, 501-1,500 members—$4.50, 1,501-2,500 members—$4.25, 2,501-5,000 members—$4.00, 5,001-10,000 members—$3.00, and over 10,000 members—$2.00. Singles copies, when available, cost $5.00; add $7.00 air mail postage to foreign countries overseas.

CHANGE OF ADDRESS. Six weeks notice is required to effect a change of address. Note your subscription number (from the mailing label), your name, and both old and new addresses, included zip codes. Please note your subscription number on the envelope. Copies will not be replaced without charge unless a request is received within 60 days of the mailing in the U.S. or within 90 days in other countries.

MARKETING DIRECTOR
Dale Griffiths

ADVERTISING ASSISTANT
Beth Binkley

ADVERTISING. Display advertising for the Journal should be arranged with the advertising representatives. RESPIRATORY CARE does not publish a classified advertising column.

ADVERTISING:
RATES AND MEDIA KITS

Aries Advertising Representatives
Saul Hornik
Sandy Getterman
12 Court St
Freehold NJ 07728
(201) 462-7422 or 972-1911

CONTENTS, *Continued*

April 1991
Volume 36, Number 4

LETTERS

315 Pulse Oximetry and Transcutaneous P_{O_2} Monitoring To Maintain Normoxia in Newborns
by Frank Monaco and Keith S Meredith—Colorado Springs, Colorado; with response by Tim Blanchette and John Dziodzio—Portland, Maine

318 Directional-Tip Catheters: Are They 'Worth the Money?'
by William R Anton—Seattle, Washington

319 Lain's Letter Expressed Personal Viewpoint
by David C Lain—Columbia, Maryland

ABSTRACTS

247 Summaries of Pertinent Articles in Other Journals

CALENDAR OF EVENTS

322 Meeting Dates, Locations, Themes

NOTICES

321 Examination Dates, Notices, Prizes

CALL FOR ABSTRACTS

323 1991 Call for Open Forum Abstracts

INFORMATION FOR AUTHORS

325 Instructions for Authors and Typists

NEW PRODUCTS

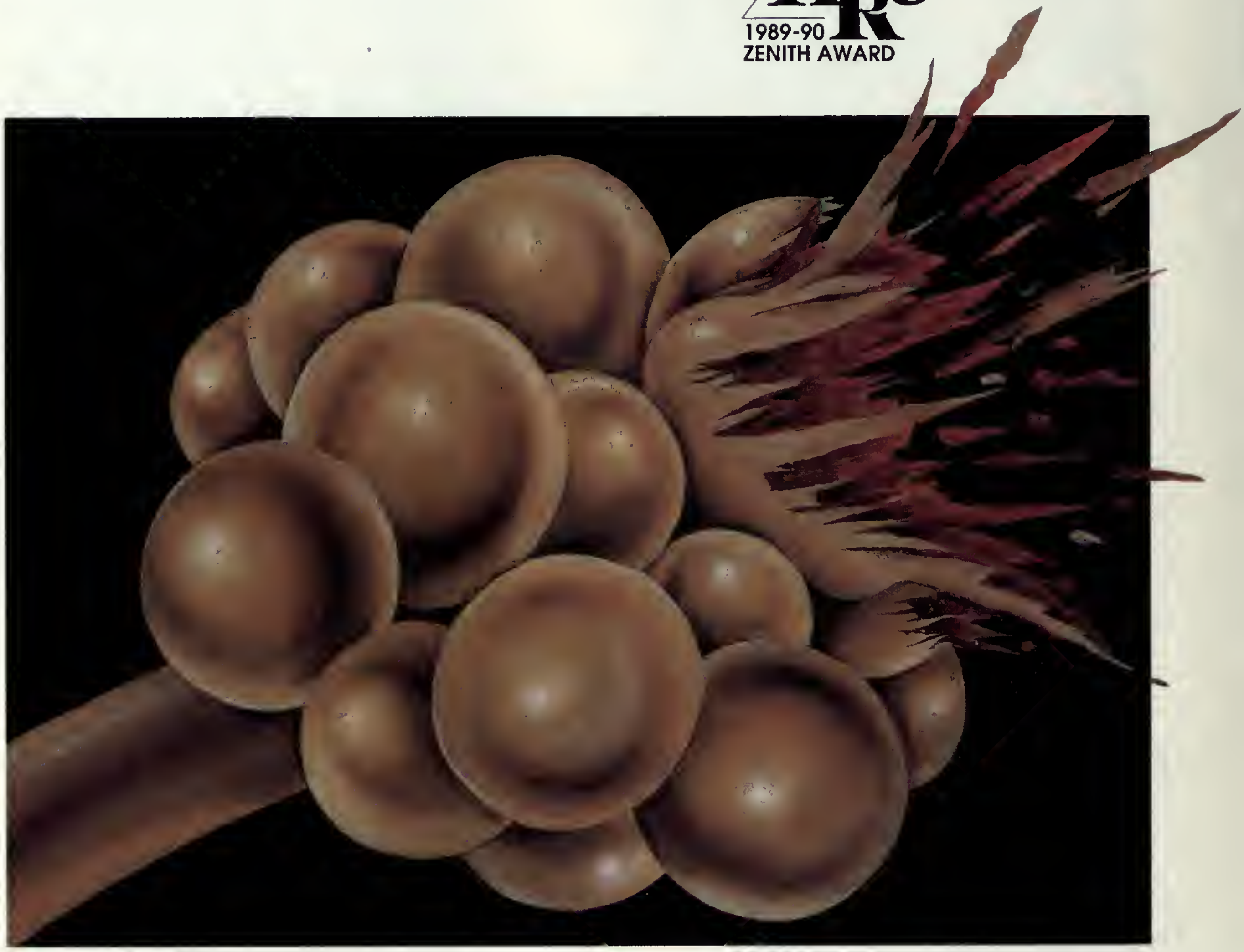
327 O_2 Concentration Monitor
327 Combination Spirometry/ECG System
327 Portable Metabolic Computer
327 Germicide/Disinfectant

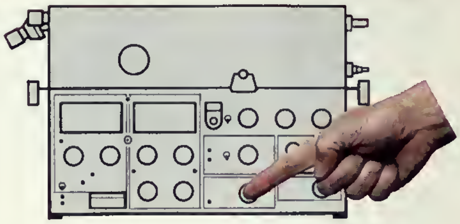
INDEXES

329 Authors in This Issue
329 Advertisers in This Issue

SIEMENS

AARC
1989-90
ZENITH AWARD

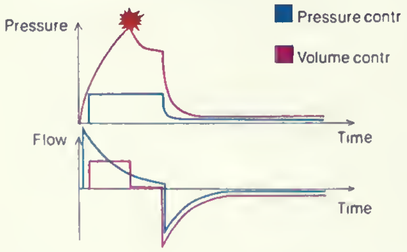




Beware!

High pressures are dangerous.

Treating a patient by means of volume ventilation can be risky. Especially when airway pressures required to deliver set volumes can increase dramatically with changing conditions.



Control pressures with Servo Pressure Controlled ventilation
With a Siemens Servo Ventilator 900C you instead can use a unique mode that controls pressure at a constant level throughout a preset inspiratory time. This combined with a decelerating flow pattern allows the opportunity for poorly ventilated lung units to expand and reopen.

Standard easy-to-use feature within every Servo 900C ventilator
No upgrades or options are required. And Siemens offers you the Servo gas delivery system allowing the capability to use Servo Pressure Controlled Ventilation on infants through adults. Instant panel access gives control at a glance.

Explore the Power of Servo...
Send for our new brochure "Only Servo!" to get a complete explanation of these unique features.

Siemens Life Support Systems
P O Box 68517, Schaumburg, Illinois 50158-0517.
Tel. (312) 397-5975, (800) 323-1281.

Life Support Systems

Circle 124 on reader service card

Reviews, Editorials, and Statements to Note

Bronchopleural Dysplasia in Adulthood (editorial)—MEB Wohl. N Engl J Med 1990;323:1834. (Pertains to the Northway et al paper abstracted below.)

Cigarette Smoking and Adolescent Pregnancy (editorial)—ER McAnarney. AJDC 1990;144:1294. (Pertains to the Davis, Tollestrup, and Milham paper abstracted below.)

High-Tech Predicament: Pulmonary Artery Catheter (editorial)—RC Bone. JAMA 1990;264:2933. (Pertains to the Iberti et al paper abstracted below.)

Research Priorities in Respiratory Nursing (statement)—American Thoracic Society. Am Rev Respir Dis 1990;142:1459.

When the Alveolus is Flooding, It's Time To Man the Pumps (editorial)—H O'Brodovich. Am Rev Respir Dis 1990;142:1247. (Pertains to the Matthay and Wiener-Kronish paper abstracted below.)

Late Pulmonary Sequelae of Bronchopulmonary Dysplasia—WH Northway Jr, RB Moss, KB Carlisle, et al. N Engl J Med 1990;323:1793.

Background. Bronchopulmonary dysplasia (BPD) is a chronic lung disease that often develops after mechanical ventilation in prematurely born infants with respiratory failure. It has become the most common form of chronic lung disease in infants in the United States. The long-term outcome for infants with BPD has not been determined. *Methods.* We studied the pulmonary function of 26 adolescents and young adults, born between 1964 and 1973, who had BPD in infancy. We compared the results with those in two control groups: 26 age-matched adolescents and young adults of similar birth weight and gestational age who had not undergone mechanical ventilation, and 53 age-matched normal subjects. *Results.* Sixty-eight percent of the subjects with BPD in infancy (17 of the 25 tested) had airway obstruction, including decreases in forced expiratory volume in one second, forced expiratory flow between 25 and 75 percent of vital capacity, and maximal expiratory flow velocity at 50 percent of vital capacity, as compared with both control groups ($p<0.0001$ for all comparisons). Twenty-four percent of the subjects with BPD in infancy had fixed airway obstruction, and 52 percent had reactive airway disease, as indicated by their responses to the administration of methacholine or a bronchodilator. Hyperinflation (an increased ratio of residual volume to total lung capacity) was more frequent in the subjects with a history of BPD than in either the matched cohort ($p<0.0006$) or the normal controls ($p<0.0004$). Six of the subjects who had BPD in infancy had severe pulmonary dysfunction or current symptoms of respiratory difficulty. *Conclusions.* Most adolescents and young adults who had BPD in infancy have some degree of pulmonary dysfunction, consisting of airway obstruction, airway hyperreactivity, and hyperinflation. The clinical consequences of this dysfunction are not known.

Trends in Teenage Smoking during Pregnancy—Washington State: 1984 through 1988—RL Davis, K Tollestrup, S Milham Jr. AJDC 1990;144:1297.

Smoking rates in the United States have decreased since 1963, but this trend is less apparent in adolescents, especially girls. Using data on birth certificates from 1984 through 1988, we analyzed smoking trends during pregnancy in teenagers in Washington State. There was a small but significant increase in the overall smoking prevalence during pregnancy between 1984 (32%) and 1988 (37%). Smoking

The new MiniCAP™ 100 CO_2 Monitor eliminates the two biggest problems in modern capnometry—calibration drift and fluid contamination.

The CO_2 monitor fo every ICU ventilator

Calibration accuracy is guaranteed with a *two-year calibration warranty*. Such enduring accuracy results from a high stability sensor design and a patented drift correction technique. The sensor's performance is monitored and, if needed, compensated for automatically, without instrument downtime or calibration gas.

The MiniCAP 100 CO_2 Monitor's fluid handling is superior, too. It features a minimal dead space fluid reservoir and fiber optics sensing that purges fluids into the reservoir, then alarms when full.

The optional MiniCAP Graphic Display Unit provides waveforms, 24-hour trend information, and digital display of CO_2, respiration rate, and mean N_2O. The unit interfaces easily with an Epson® FX graphics compatible printer for hard copy of waveforms.

For complete details on the CO_2 monitor you can use with confidence, call **1-800-672-4678**, Ext. 8826.

MSA CATALYST RESEARCH

3706 Crondall Lane
Owings Mills, MD 21117 USA
301/356-2400
FAX: 301/581-0346

Circle 127 on reader service card

Epson is a registered trademark of Seiko Epson Corporation.

rates varied by mother's age, race and ethnicity, marital status, and prenatal care. Whites had the highest smoking prevalence, and native Americans showed the largest increase in smoking prevalence over time. In the 5 years studied, unmarried pregnant teenagers had a smoking prevalence of 42.8%, compared with a rate of 31.7% in married teenagers. Compared with other studies of smoking rates in nonpregnant teenagers, pregnant teenagers in Washington State had a much higher smoking prevalence than their nonpregnant peers, and the differences between these two groups did not appear to diminish over time. This study suggests that there is little movement toward meeting the *1990 Health Objectives for the Nation* regarding smoking in Washington State teenagers who become pregnant.

A Multicenter Study of Physicians' Knowledge of the Pulmonary Artery Catheter—TJ Iberti, EP Fischer, AB Leibowitz, EA Panacek, JH Silverstein, TE Albertson, and the Pulmonary Artery Catheter Study Group. JAMA 1990:264:2928.

We administered a 31-question multiple-choice examination to 496 physicians practicing in 13 medical facilities in the United States and Canada to asssess their knowledge and understanding of the use of the pulmonary artery catheter and interpretation of data derived from it. The mean test score was 20.7 (67% correct), with an SD of 5.4 and a range of 6 to 31 (19% to 100%). Mean scores varied independently by training, frequency of use of pulmonary artery catheter data in patient treatment, frequency of inserting a pulmonary artery catheter, and whether the respondent's hospital was a primary medical school affiliate. Given the variability in physician understanding of the pulmonary artery catheter, we believe that credentialing policies should be reevaluated and that consideration should be given to restricting its use to individuals with documented competency.

Intact Epithelial Barrier Function is Critical for the Resolution of Alveolar Edema in Humans—MA Matthay, JP Wiener-Kronish. Am Rev Respir Dis 1990;142:1250.

Within 15 min of endotracheal intubation, the resolution of pulmonary edema was studied over the next 12 h in 34 mechanically ventilated patients by (1) serial measurements of the alveolar-arterial oxygen difference, (2) the extent of edema on the initial and follow-up chest radiograph, and (3) by an initial and final measurement of total protein and albumin concentration in sequential samples of pulmonary edema fluid. Based on the oxygenation and chest radiographic data, 24 patients clinically improved and 10 patients did not improve. In the 10 patients who did not clinically improve (3, hydrostatic edema; 7, permeability edema), there was no change in the final edema fluid protein concentration (4.1 ± 1.1 g/100 mL) compared with the initial edema fluid protein concentration (4.2 ± 1.0 g/100 mL) (p = ns). However, in the 24 patients who clinically improved (15, hydrostatic edema; 9, permeability edema), there was an increase in every patient's final edema protein concentration (5.6 ± 2.3 g/100 mL) compared with their initial edema protein concentration (3.8 ± 1.2 g/100 mL) ($p < 0.01$). In 13 of these 24 patients, the final edema fluid concentration (7.3 ± 1.6 g/100 mL) exceeded the final plasma protein concentration (5.6 ± 0.8 g/100 mL) by a mean value of 1.7 g/100 mL protein. The data provide the first evidence in humans to support the hypothesis that active ion transport across the alveolar epithelial barrier is the primary mechanism for clearance of edema fluid from the air spaces of the lung. In addition, the use of sequential pulmonary edema fluid protein concentration as an index of alveolar epithelial barrier function provided a good prognostic indicator of survival in the 16 patients with increased permeability pulmonary edema.

Home Care for Ventilator-Dependent Children—RD Quint, E Chesterman, LS Crain, M Winkleby, WT Boyce. AJDC 1990;144:1238.

The impact of providing home care for ventilator-dependent children was studied in a cross-sectional survey of 18 northern California families. Through the use of a confidential structured interview and the Impact on the Family Scale, we obtained information on family demographics; the childrens' medical conditions; financial, social, and personal impact on the family; and parental coping-mastery of the care of a ventilator-dependent child at home. Analysis of scores from the impact on Family Scale showed no differences in the perceived family impact between primary caretakers and their spouses. Primary caretakers in the sample, however, showed significantly reduced Coping subscale scores with a longer duration of home ventilatory care. This finding, if confirmed in future studies, has policy implications for physicians and other health professionals working with ventilator-dependent children and their families, especially those who care for children over long periods.

Aerosolised Ribavarin in Infants Requiring Mechanical Ventilation for Severe Lower Respiratory Tract Infection Caused by Respiratory Syncytial Virus—DW Smith, LR Frankel, LH Mathers, ATS Tang, RL Ariagno, CG Prober. Clin Res 1991;39(1):59A.

We conducted a placebo-controlled, blinded, randomised trial of aerosolised ribavirin in infants requiring mechanical ventilation (MV) for respiratory failure ($P_{aCO_2} > 60$ torr,

QUALITY BY DESIGN.

Blood Gas/ Hemoglobin Analyzers

AVL's uncompromising commitment is to provide the highest quality Blood Gas Analyzers and CO-Oximeters through state-of-the-art technology and unsurpassed reliability.

The full line of AVL instruments is designed to satisfy every laboratory need. The AVL model 995, and the economical 990, for pH, PO_2 and PCO_2. AVL 995 Hb combines all the AVL 995 capabilities plus Total Hemoglobin. The AVL 912 CO-Oxylite measures hemoglobin fractions and reports calculated parameters.

Of course, the AVL 995 and 995 Hb interface with the complete line of AVL Electrolyte Analyzers to provide fully integrated BGA and electrolyte reports.

Advanced technology is designed into each analyzer to deliver the lowest annual operating cost and allow full testing of samples as small as 25 μL.

The most comprehensive service coverage available is provided through the AVL ADVANTAGE PROGRAM:

- The *only* five year, full-service warranty.
- 24 hour-a-day telephone technical support.
- 24 hour-a-day, on-line, computer aided instrument diagnostics via a modem. It's called TeleLink.
- Coast-to-coast field technical service representatives.

AVL analyzers are the preferred choice of hospitals, clinics and laboratories worldwide. For more information about the complete line of quality analyzers and the exclusive *five year, full-service warranty,* write AVL Scientific Corporation, P.O. Box 337, 33 Mansell Court, Roswell, GA 30077, or call toll-free (800) 421-4646. In Georgia, (404) 587-4040.

AVL

Circle 104 on reader service card

$P_{aO_2} < 60$ torr with $F_{IO_2} > 0.6$) or respiratory arrest due to respiratory syncytial virus (RSV). Ribavirin (R) or sterile water placebo (P) was delivered by continuous aerosolisation into the MV circuit for the duration of MV support or for 7 days, whichever was shorter. Twenty-eight infants (mean age 1.4 ± 1.7 months) were enrolled; 7 had underlying diseases predisposing to severe infection, and 21 were previously normal, but young, with a mean age of 0.8 ± 0.9 months. Fourteen infants received R and 14 received P. There were no differences between the 2 groups in age, sex distribution, underlying diseases, or in duration of illness prior to admission. The 2 groups also were comparable for MV rate, peak inspiratory pressure, F_{IO_2}, P_{aO_2}, and P_{aCO_2} prior to the initiation of therapy. The duration of MV and of supplemental O_2 use were significantly decreased for the R-treated group. Furthermore, considering only the 21 previously normal infants, duration of hospital stay was significantly shortened for those who received R.

Ribavirin
n—14
Days MV—4.9 ± 3.7
Days O_2—8.7 ± 6.0
Days hospital stay (normal)—10.2± 5.3

Placebo
n—14
Days MV—9.9 ± 5.6*
Days O_2—13.5 ± 5.0*
Days hospital stay (normal)—16.0± 5.4*

---

*$p < 0.05$

Two infants, both of whom were receiving P, worsened during treatment and met pre-established exit criteria on the fifth day of the study. One of these infants died. We conclude that ribavirin decreases the duration of MV and oxygen treatment, and the length of hospital stay, in infants with severe RSV infection requiring MV.

Biodistribution, Tissue Reaction, and Lung Retention of Pentamidine Aerosolized as Three Different Salts—R Debs, E Brunette, H Fuchs, Am Rev Respir Dis 1990;142:1164.

Aerosolized pentamidine isoethionate is retained in the lung and appears to prevent *Pneumocystis carinii* pneumonia (PCP) in many AIDS patients. We evaluated alternative formulations of pentamidine that might reduce the airway irritation associated with aerosolized pentamidine isoethionate. Specifically, we assessed the biodistribution, histologic response, and lung retention of the isoethionate, gluconate, and lactate salts of pentamidine after aerosol administration to mice. For each of the three aerosolized salts tested, greater than 50% of the pentamidine initially recovered from the lungs after one dose was still retained there 14 days later. Thus, significant levels of pentamidine, aerosolized as three different salts, are retained in the lung for at least 2 weeks after a single dose. The three salts of pentamidine each produced high lung-to-extrapulmonary-drug ratios, the converse of that produced by intravenous injection of pentamidine isoethionate. At very high aerosol doses, the ability of the lung to retain pentamidine appeared saturable. Even aerosolized daily for 2 weeks at very high doses, none of the three pentamidine salts produced histologic evidence of organ toxicity. A Phase 1 trial of aerosolized pentamidine gluconate in AIDS-PCP patients is now in progress to determine if this approach can reduce airway irritation.

Tolerance and Dependence in Neonates Sedated with Fentanyl during Extracorporeal Membrane Oxygenation—JH Arnold, RD Truog, EJ Ora, JM Scavone, MB Hershenson. Anesthesiology 1990;73:1136.

We undertook a retrospective chart review of 37 neonates who received fentanyl by continuous infusion while undergoing extracorporeal membrane oxygenation (ECMO) between May 1986 and October 1988. We quantified the doses of all sedatives utilized, determined the incidence of neonatal abstinence syndrome (NAS), and identified risk factors associated with NAS. We determined peak fentanyl infusion rate, mean fentanyl infusion rate, total fentanyl dose, and duration of ECMO therapy. NAS was observed in 21 of 37 neonates (57%). In both the NAS and non-NAS neonates, mean infusion rate increased steadily during ECMO therapy, from a mean of 11.6 ± 6.9 (SD) $\mu g \cdot kg^{-1} \cdot h^{-1}$ on Day 1 to a mean of 52.5 ± 19.4 (SD) $\mu g \cdot kg^{-1} \cdot h^{-1}$ by Day 8. Total fentanyl dose and duration of ECMO were significantly greater in neonates with NAS. We found that neonates with a total dose > 1.6 mg/kg or an ECMO duration > 5 days had a significantly greater incidence of NAS (chi-squared test; $p < 0.01$ and $p < 0.005$; odds ratios = 7.0 and 13.9, respectively). With multiple logistic regression, ECMO duration was found to be the most powerful predictor of the occurrence of NAS. We also measured plasma fentanyl concentrations in a separate group of 5 neonates receiving fentanyl by continuous infusion for sedation. Fentanyl concentrations increased steadily during the period of infusion, suggesting the development of tolerance to the sedating effects. We conclude that continuous administration of fentanyl for sedation is associated with the uniform development of tolerance and a significant incidence of dependence. Alternative approaches to sedation should be investigated.

Manual Ventilation Bags as a Source for Bacterial Colonization of Intubated Patients—DJ Weber, MB Wilson, WA Rutala, CA Thomann. Am Rev Respir Dis 1990;142:892.

A group of 14 intensive care (ICU) patients were studied to determine if manual ventilation bags (MVB) could serve as a source of bacterial or fungal pathogens that could colonize the respiratory tract of intubated patients. A total of 51 cultures were simultaneously obtained of patient's sputum, the exterior MVB surface, MVB port, and MVB interior (postexhalation valve). Pathogens colonizing or infecting the respiratory tract of intubated ICU patients were frequently simultaneously present on the exterior surface of the MVB and inside the MVB port used to connect the MVB with the endotracheal tube. In addition, coagulase-negative staphylococci and yeast were frequently present on the exterior surface of the MVB. The interior of the MVB was usually sterile. In three instances, pathogens were isolated from the MVB before isolation from the patient's sputum. MVB may serve as a source for colonizing the respiratory tract of intubated ICU patients and/or the hands of medical personnel. The exterior surface and port of MVB should be cleaned of visible debris and disinfected at least once a day.

Diaphragmatic Rest during Negative Pressure Ventilation by Pneumowrap—S Nava, N Ambrosino, L Zocchi, C Rampulla. Chest 1990;98:857.

In the present study, we assessed the occurrence of respiratory muscle rest during long-lasting, intermittent negative pressure ventilation (INPV) runs using a pneumowrap ventilator at different pressure levels. We measured two indices of diaphragmatic activity: transdiaphragmatic (P_{di}) pressure and the electrical activity of the diaphragm (E_{di}). Five healthy volunteers and six COPD patients were studied during spontaneous breathing and during 30-minute runs of INPV at pressures of –2, –15, and –30 cm H_2O. Ventilation, rib-cage, and abdomen motion were measured by inductive plethysmography; P_{di} was obtained as the difference between gastric and esophageal pressures; E_{di} was recorded with surface electrodes. About 10 minutes of INPV (adaptation phase) were needed to obtain stable values in all the variables recorded. Ventilation increased in both groups up to threefold by increasing the negative pressure applied, this being due to changes in tidal volume. Changes in gastric pressure (P_{ga}) swings mainly accounted for the reduction in P_{di} that became negative during the run at –30 cm H_2O. In both groups, E_{di}, after adaptation, showed no change during INPV at –2 cm H_2O but a progressive reduction from control, during INPV at –15 and –30 cm H_2O. We conclude that INPV by a pneumowrap ventilator can induce partial respiratory muscle rest in normal subjects and COPD patients.

WHY LET YOUR PATIENTS MIX THEIR MEDICATIONS AND PAY FOR THEM?

X-ACT DOSE Respiratory Services Takes Care of Everything

NO BILLING • NO RISK • NO COST TO PATIENTS *

No cost to the patient, fully covered by Medicare and Secondary.*

No more confusion. All medications are premixed and premeasured with a pharmaceutical accuracy you can depend on.

X-ACT DOSE Respiratory Services fills out the forms, then we bill Medicare and Secondary.*

JAWS clause - If stolen or spilled, or a shark comes out of the water and bites it, medication is free, replacement is free and sent Federal Express next morning.

Arthritic-oriented easy-open vial.

If your patient has a problem visually measuring or physical impairment, delivery of the medication is easy and error free.

* Ask about our dealer billing options.
* No cost applies when patient has Part B and a medigap secondary insurance.

1-800-367-9228 1-800-367-9228

Circle 149 on reader service card

New

2500

VOLDYNE®

Volumetric Incentive Deep-Breathing Exerciser

The accuracy of Voldyne, in a new size, matched to geriatric patients and patients with smaller lung capacities.

Voldyne 2500 . . .

- A smaller, lighter flow cup **reduces the work of breathing**, thus improving patient performance and progress.
- Every unit is **individually tested and calibrated** for performance, reliability and superior accuracy of inhaled lung volume.
- Volume incentive spirometry **improves assessment of patient progress** by eliminating the guesswork associated with spirometers that only measure flow.
- Graduations printed on both sides of the unit allow the therapist to conveniently **observe volumes while instructing and encouraging the patient.**

For further information, contact your Sherwood O.R. / Critical Care Representative or call:

1-800-325-7472 (outside Missouri)
1-800-392-7318 (in Missouri)

©1991 Sherwood Medical Company

Sherwood
MEDICAL
ST LOUIS, MO 63103 USA

Circle 139 on reader service card

Thanks to Ohmeda, you'll never lose sight of what's important.

AARC
1990
ZENITH AWARD

When you're monitoring critical care patients, you need a complete view of their respiratory status. And now there's an easy way to get it. The OxiCap Monitor from Ohmeda.

At a glance, it gives you pulse oximetry, capnography and inspired oxygen readings. Continuously. So you can make minor adjustments rather than radical changes. And it's designed for the demanding environment of critical care.

Along with the OxiCap Monitor, we bring you over 80 years of experience developing products for critical care. So call us today. And get a much clearer picture of your patients.

Ohmeda
We monitor life.

1315 West Century Drive
Louisville CO 80027 USA
To order: 1 800 345 2700

A Division of The BOC Group Inc

A BOC Health Care Company
Critical Care Worldwide

©[illegible] The BOC Group Inc

Circle 110 on reader service card

Compliance, Alveolar-Arterial Oxygen Difference, and Oxygenation Index Changes in Patients Managed with Extracorporeal Membrane Oxygenation—DS Brudno, RF Boedy, WP Kanto Jr. Pediatr Pulmonol 1990;9:19-23.

Eighteen patients with meconium aspiration syndrome who failed conventional management were treated with extracorporeal membrane oxygenation (ECMO) for reversible respiratory failure. Dynamic lung compliance measurements were made prior to, during, and after ECMO support. $P(A-a)_{O2}$ and oxygenation index (OI) measurements were calculated prior to and after ECMO support. Lung compliance decreased significantly comparing before-ECMO to during-ECMO, and increased significantly comparing during- to after-ECMO, but not comparing before- to after-ECMO measurements. $P(A-a)_{O2}$ and OI decreased significantly from before to after ECMO. The improvement in oxygenation allowing removal from ECMO does not appear to be related to improved pulmonary mechanics, but may rather be secondary to increased effective pulmonary capillary blood flow.

Distinguishable Types of Dyspnea in Patients with Shortness of Breath—PM Simon, RM Schwartzstein, JW Weiss, V Fencl, M Teghtsoonian, SE Weinberger. Am Rev Respir Dis 1990;142:1009.

Dyspnea frequently accompanies a variety of cardiopulmonary abnormalities. Although dyspnea is often considered a single sensation, alternatively it may encompass multiple sensations that are not well explained by a single physiologic mechanism. To investigate whether breathlessness experienced by patients represents more than one sensation, we studied 53 patients with one of the following seven conditions: pulmonary vascular disease, neuromuscular and chest wall disease, congestive heart failure, pregnancy, interstitial lung disease, asthma, and chronic obstructive pulmonary disease. Patients were asked to choose descriptions of their sensation(s) of breathlessness from a dyspnea questionnaire listing 19 descriptors. Cluster analysis was used to identify natural groupings among the chosen descriptors. We found that patients could distinguish different sensations of breathlessness. In addition, we found an association between certain groups of descriptors and specific conditions producing dyspnea. These findings concur with those in an earlier study in normal volunteers in whom dyspnea was induced by various stimuli. We conclude that different types of dyspnea exist in patients with a variety of cardiopulmonary abnormalities. Furthermore, different mechanisms may mediate these various sensations.

Effect of Corticosteroids on Respiratory Muscle Histopathology—GT Ferguson, CG Irvin, RM Cherniack. Am Rev Respir Dis 1990;142:1047.

Pathologic alterations induced by corticosteroid administration were evaluated in the respiratory muscles and compared to those in the peripheral skeletal muscles of the rabbit. Alterations in gross and microscopic pathology as well as histochemistry were determined in the diaphragm, intercostal, sternocleidomastoid, extensor digitorum longus, and soleus muscles following 3 weeks of intramuscular cortisone injections. Corticosteroid administration induced significant pathologic changes in all the muscles except the soleus. Although gross pathologic changes were greatest in the extensor digitorum longus, microscopic changes were greatest in the diaphragm. Reductions in total muscle-fiber volume were similar in the diaphragm, sternocleidomastoid, and etensor digitorum longus muscles. The composition of muscle-fiber types and the number of fibers in a muscle were not altered in any of the muscles studied following corticosteroids. There was significant atrophy of individual muscle fibers in all the muscles except the soleus. In the diaphragm, corticosteroids induced atrophy of all fiber types, including Type I fibers. Atrophy of Type I fibers was not present in the peripheral skeletal muscles or the other respiratory muscles. On the other hand, corticosteroids induced selective atrophy of Type IIb muscle fibers in the intercostal and sternocleidomastoid muscles similar to that in the peripheral skeletal muscles. These findings suggest that the effect of corticosteroids on the diaphragm is unique, and one cannot extrapolate from the effect of corticosteroids on peripheral skeletal muscles to that in the diaphragm. In addition, these pathologic changes may have functional relevance, since atrophy of Type I fibers may result in a reduction in muscle endurance.

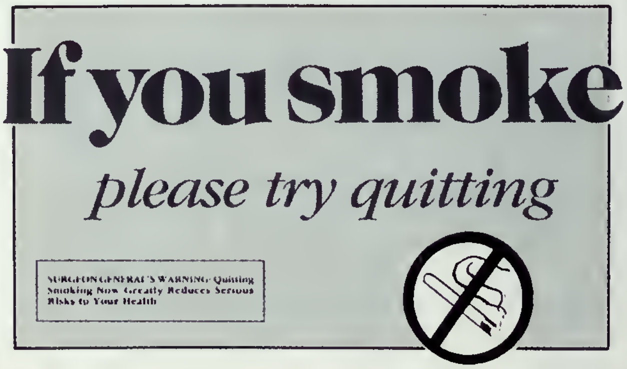
HEED THE CALL!

1991 Call For Open Forum Abstracts

Page 323

Smokers Need YOU
to help them quit
Now You Can help with. . .
IF YOU SMOKE...PLEASE TRY QUITTING

The AARC has teamed up with California College for Health Sciences to offer you a "no gimmick" approach to help the smoker who wants to quit or whose life depends on quitting. Based on sound psychological principles, *If You Smoke...* offers information to aid you in helping your patients overcome both the physical addiction and psychological dependency of smoking. By Patricia Scheiderman and Dr. Stan Lederman, *If You Smoke...* is a result of years of research and teaching by Lederman, a clinical psychologist and former smoker.


If you smoke
please try quitting
SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health

If You Smoke... incorporates all the elements of a successful smoking cessation program — proven in a clinical setting, in four parts that help the smoker focus on the benefits of quitting instead of negative aspects:

- Preparing to Quit
- Learning the Right Way To Quit
- Setting Yourself Up For Success
- Quitting For Life

Other tools for relieving anxiety after quitting and learning how to deal with irritability and other problems facing the new non-smoker are also a part of the *If You Smoke...* program. The 60-minute audio tape will take the participant through a progressive relaxation program helping the smoker relieve the new tension of quitting.

Health promotion and disease prevention is certainly one of your goals but you will also be able to fulfill important continuing education requirements by completing this two-session six CEU course that will qualify you to conduct a smoking cessation program for your patients.

The program includes an instructor's manual, workbook, and companion audio tape and costs less than what an average smoker spends on cigarettes in five weeks.

Materials for your patients participating in the *If You Smoke...* smoking cessation program includes the workbook and 60-minute companion tape.

Item BK13-Instructor's Kit - includes manual, workbook, and 60-minute companion audio tape - $70 (AARC Members Pay Only $60)
Item BK14 - Participant's Kit - includes workbook and 60-minute companion audio tape - $28 (AARC Members Pay Only $18)

I want to help my patients quit smoking.
Send me:

_______ copy(ies) of *If you Smoke....* Instructor Kit—$70 (Members $60) BK13
_______ copy(ies) of *If you Smoke....* Participant Kit —$28 (Members $18) BK14

☐ Payment is enclosed in the amount of $ ________________
☐ Bill me, my purchase order number is ________________
Charge to my ☐ Visa, ☐ MasterCard.
Number ________________ Exp. Date ________________

Signature ________________

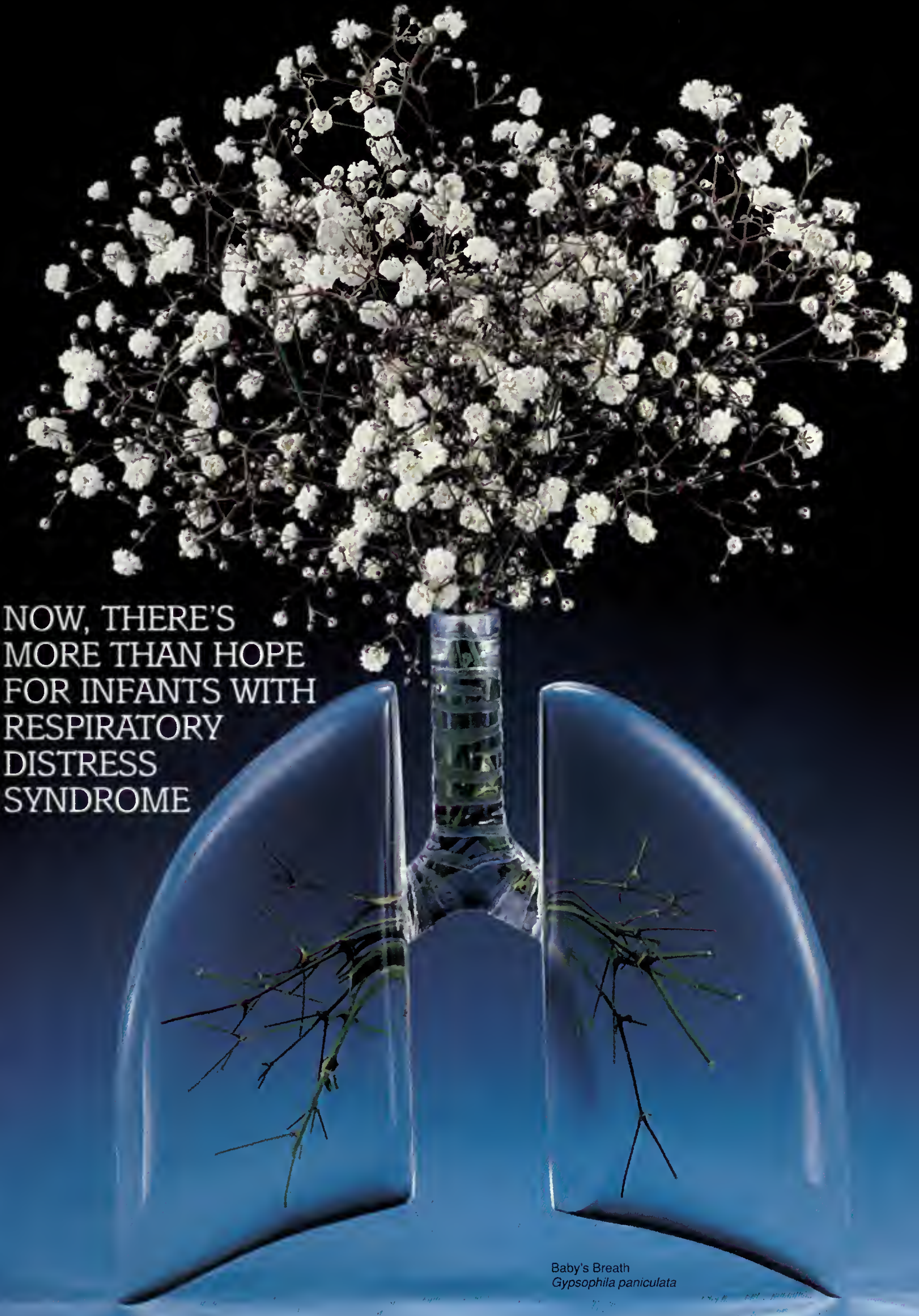
Name ________________

Address ________________

City ________________ State ________ Zip ________________

AARC Member Number (necessary for AARC member price) ________________

Mail to The AARC, 11030 Ables Lane, Dallas, TX 75229



NOW, THERE'S MORE THAN HOPE FOR INFANTS WITH RESPIRATORY DISTRESS SYNDROME
Baby's Breath
Gypsophila paniculata

New, protein-free synthetic lung surfactant that's as easy to use as it is effective

Exosurf® NEONATAL™
(Colfosceril Palmitate, Cetyl Alcohol,
Tyloxapol) For Intratracheal Suspension

At last, there's more than hope for infants with respiratory distress syndrome (RDS). Clinical trials have shown that protein-free synthetic EXOSURF Neonatal dramatically reduced neonatal morbidity and mortality. In addition to being effective in both prophylactic and rescue use, EXOSURF Neonatal was well tolerated.

Widely studied

To date, in excess of 2,600 premature infants have received EXOSURF Neonatal in controlled clinical trials involving more than 4,400 infants in North America. In addition, 10,000 infants in more than 400 hospitals have received EXOSURF Neonatal under a treatment IND.

Effective in infants at risk of developing RDS

A single, prophylactic dose of EXOSURF Neonatal given immediately following birth reduced death from RDS by 50% and one-year mortality by 33% in neonates weighing 700 to 1100 grams. Two additional prophylactic doses of EXOSURF Neonatal reduced one-year mortality by an additional 30%. EXOSURF Neonatal reduced the severity of RDS and the incidence of lung rupture in these premature infants.

Effective in infants with RDS

In infants weighing 700 to 1350 grams, EXOSURF Neonatal rescue treatment initiated within 24 hours of birth, reduced death from RDS by 66% and one-year mortality by 44%. Survival to day 28 without bronchopulmonary dysplasia was increased significantly. Pneumothorax, pulmonary interstitial emphysema, and overall pulmonary air leaks were significantly reduced. Similarly beneficial effects were also observed in infants with RDS weighing >1350 grams, and chronic lung disease was significantly reduced.

Impressive safety profile

In individual controlled clinical trials, adverse events were comparable to those of placebo, with the exception of apnea. Infants receiving EXOSURF Neonatal required less ventilatory support, possibly contributing to an increased incidence of apnea. In both placebo and treated infants, apnea proved to be a marker for reduced pulmonary air leak and improved survival.

In the treatment IND experience of over 10,000 infants, the reported incidence of pulmonary bleeding was 4%. It appears to be related to improvements in pulmonary function in infants whose ductus arteriosus remains patent. This condition may be prevented by early and aggressive diagnosis and treatment (unless contraindicated) of patent ductus arteriosus during the first two days of life (while the ductus arteriosus is often clinically silent). Additionally, a low incidence (3/1,000) of mucous plugging of the endotracheal tube was observed.

Please see full prescribing information on last pages of this advertisement.

Exosurf® NEONATAL™
(Colfosceril Palmitate, Cetyl Alcohol,
Tyloxapol) For Intratracheal Suspension

Easy to store

- EXOSURF Neonatal may be stored at room temperature (15° to 30°C [59° to 86°F]).
- Reconstituted suspension may be maintained refrigerated or at room temperature (2° to 30°C [36° to 86°F]) for up to 12 hours.

Easy to use

- Key items needed for EXOSURF Neonatal administration are supplied in one carton: one 10 mL vial of EXOSURF Neonatal, one 10 mL vial of Sterile Water for Injection, and five endotracheal tube adapters (2.5 mm, 3.0 mm, 3.5 mm, 4.0 mm, and 4.5 mm).

Easy to administer

- Each EXOSURF Neonatal dose is administered in two 2.5 mL/kg half-doses.
- EXOSURF Neonatal is administered via a sideport on a special endotracheal tube adapter (supplied with EXOSURF Neonatal) without interrupting mechanical ventilation.

Easy on the infant

- To assist the distribution of EXOSURF Neonatal in the lungs, the infant is simply turned from midline position to the right after the first half-dose and from midline position to the left after the second half-dose.

A complimentary videotape on reconstitution and administration of EXOSURF Neonatal is available from your Burroughs Wellcome Co. representative.

Please see full prescribing information on last pages of this advertisement. Call your Burroughs Wellcome Co. professional representative for further information.

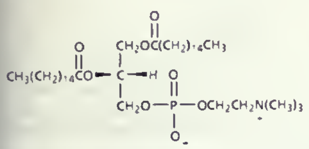
Wellcome Copr. © 1990 Burroughs Wellcome Co. All rights reserved. EX112

EXOSURF® (COLFOSCERIL PALMITATE, CETYL ALCOHOL, TYLOXAPOL)
Neonatal For Intratracheal Suspension

DESCRIPTION: Exosurf Neonatal for Intratracheal Suspension is a protein-free synthetic lung surfactant stored under vacuum as a sterile lyophilized powder. Exosurf Neonatal is reconstituted with preservative-free Sterile Water for Injection prior to administration by intratracheal instillation. Each 10 mL vial contains 108 mg colfosceril palmitate, commonly known as dipalmitoylphosphatidylcholine (DPPC), formulated with 12 mg cetyl alcohol, 8 mg tyloxapol, and 47 mg sodium chloride. Sodium hydroxide or hydrochloric acid may have been added to adjust pH. When reconstituted with 8 mL Sterile Water for Injection, the Exosurf Neonatal suspension contains 13.5 mg/mL colfosceril palmitate, 1.5 mg/mL cetyl alcohol, and 1 mg/mL tyloxapol in 0.1 N NaCl. The suspension appears milky white with a pH of 5 to 7 and an osmolality of 185 mOsm/L.

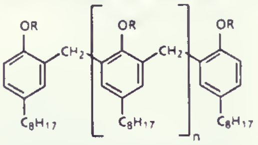
The chemical names and structural formulas of the components of Exosurf Neonatal are as follows:

colfosceril palmitate
(1,2-dipalmitoyl-sn-3-phosphoglycerocholine)



cetyl alcohol
(1-hexadecanol)
$CH_3(CH_2)_{14}CH_2OH$

tyloxapol
(formaldehyde polymer with oxirane and 4-(1,1,3,3-tetramethylbutyl)phenol)



[R is $CH_2CH_2O(CH_2CH_2O)_mCH_2CH_2OH$; m is 6 to 8; n is not more than 5]

CLINICAL PHARMACOLOGY: Surfactant deficiency is an important factor in the development of the neonatal respiratory distress syndrome (RDS). Thus, surfactant replacement therapy early in the course of RDS should ameliorate the disease and improve symptoms. Natural surfactant, a combination of lipids and apoproteins, exhibits not only surface tension reducing properties (conferred by the lipids), but also rapid spreading and adsorption (conferred by the apoproteins). The major fraction of the lipid component of natural surfactant is DPPC, which comprises up to 70% of natural surfactant by weight.

Although DPPC reduces surface tension, DPPC alone is ineffective in RDS because DPPC spreads and adsorbs poorly. In Exosurf Neonatal, which is protein free, cetyl alcohol acts as the spreading agent for the DPPC on the air-fluid interface. Tyloxapol, a polymeric long-chain repeating alcohol, is a nonionic surfactant which acts to disperse both DPPC and cetyl alcohol. Sodium chloride is added to adjust osmolality.

Pharmacokinetics: Exosurf Neonatal is administered directly into the trachea. Human pharmacokinetic studies of the absorption, biotransformation, and excretion of the components of Exosurf Neonatal have not been performed. Nonclinical studies, however, have shown that DPPC can be absorbed from the alveolus into lung tissue where it can be catabolized extensively and reutilized for further phospholipid synthesis and secretion. In the developing rabbit, 90% of alveolar phospholipids are recycled. In premature rabbits, the alveolar half-life of intratracheally administered H^3-labeled phosphatidylcholine is approximately 12 hours.

Animal Studies: In animal models of RDS, treatment with Exosurf Neonatal significantly improved lung volume, compliance and gas exchange in premature rabbits and lambs. The amount and distribution of lung water were not affected by Exosurf Neonatal treatment of premature rabbit pups. The extent of lung injury in premature rabbit pups undergoing mechanical ventilation was reduced significantly by Exosurf Neonatal treatment. In premature lambs, neither systemic blood flow nor flow through the ductus arteriosus were affected by Exosurf Neonatal treatment. Survival was significantly better in both premature rabbits and premature lambs treated with Exosurf Neonatal.

Clinical Studies: Exosurf Neonatal has been studied in the U.S. and Canada in controlled clinical trials involving more than 4400 infants. Over 10,000 infants have received Exosurf Neonatal through an open, uncontrolled, North American study designed to provide the drug to premature infants who might benefit and to obtain additional safety information (Exosurf Neonatal Treatment IND).

Prophylactic Treatment: The efficacy of a single dose of Exosurf Neonatal in prophylactic treatment of infants at risk of developing respiratory distress syndrome (RDS) was examined in three double-blind, placebo-controlled studies, one involving 215 infants weighing 500 to 700 grams, one involving 385 infants weighing 700 to 1350 grams, and one involving 446 infants weighing 700 to 1100 grams. The infants were intubated and placed on mechanical ventilation, and received 5 mL/kg Exosurf Neonatal or placebo (air) within 30 minutes of birth.

The efficacy of one versus three doses of Exosurf Neonatal in prophylactic treatment of infants at risk of developing RDS was examined in a double-blind, placebo-controlled study of 823 infants weighing 700 to 1100 grams. The infants were intubated and placed on mechanical ventitation, and received a first 5 mL/kg dose of Exosurf Neonatal within 30 minutes. Repeat 5 mL/kg doses of Exosurf Neonatal or placebo (air) were given to all infants who remained on mechanical ventilation at approximately 12 and 24 hours of age. An initial analysis of 716 infants is available.

The major efficacy parameters from these studies are presented in Table 1.

Table 1 **Efficacy Assessments—Prophylactic Treatment**

Number of Doses: Birth Weight Range:	Single Dose 500 to 700 grams		Single Dose 700 to 1350 grams		Single Dose 700 to 1100 grams		One Versus Three Doses 700 to 1100 grams	
Treatment Group:	Placebo (Air)	EXOSURF	Placebo (Air)	EXOSURF	Placebo (Air)	EXOSURF	One EXOSURF Dose	Three EXOSURF Doses
Number of Infants:	N=106	N=109	N=185	N=176	N=222	N=224	N=356	N=360
	% of Infants		% of Infants		% of Infants		% of Infants	
Death ≤ Day 28[a]	53	50	11	6	21	15	16	9*
Death through 1 Year[a]	59	60	14	11	30	20**	17	12*
Death from RDS[b]	25	13*	4	3	10	5§	3	2
Intact Cardiopulmonary Survival[a,c]	29	25	69	78*	65	68	74	78
Bronchopulmonary Dysplasia (BPD)[a,d]	43	44	23	18	19	21	8	12
RDS Incidence[b]	73	81	46	42	55	55	63	68

[a] "Intent-to-treat" analyses (as randomized) except for the 700 to 1350 gram, single dose study in which patients with congenital infections and anomalies were excluded
[b] "As-treated" analyses
[c] Defined by survival through 28 days of life without bronchopulmonary dysplasia
[d] Defined by a combination of clinical and radiographic criteria

* $p<0.05$
** $p<0.01$
§ $p=0.051$

Rescue Treatment: The efficacy of Exosurf Neonatal in the rescue treatment of infants with RDS was examined in two double-blind, placebo-controlled studies. One study enrolled 419 infants weighing 700 to 1350 grams; the second enrolled 1237 infants weighing 1250 grams and above. In the rescue treatment studies, infants received an initial dose (5 mL/kg) of Exosurf Neonatal or placebo (air) between 2 and 24 hours of life followed by a second dose (5 mL/kg) approximately 12 hours later to infants who remained on mechanical ventilation. The major efficacy parameters from these studies are presented in Table 2.

Table 2 **Efficacy Assessments—Rescue Treatment**

Number of Doses: Birth Weight Range:	Two Doses 700 to 1350 grams		Two Doses 1250 grams and above	
Treatment Group:	Placebo (Air)	EXOSURF	Placebo (Air)	EXOSURF
Number of Infants:	N=213	N=206	N=623	N=614
	% of Infants		% of Infants	
Death ≤ Day 28[a]	23	11***	7	4*
Death through 1 Year[a]	27	15***	9	6§
Death from RDS[b]	10	3**	3	1*
Intact Cardiopulmonary Survival[a,c]	62	75**	88	93**
Bronchopulmonary Dysplasia (BPD)[a,d]	18	15	6	3*

[a] "Intent-to-treat" analyses (as randomized)
[b] "As-treated" analyses
[c] Defined by survival through 28 days of life without bronchopulmonary dysplasia
[d] Defined by a combination of clinical and radiographic criteria

* $p<0.05$
** $p<0.01$
*** $p<0.001$
§ $p=0.067$

Clinical Results: In these six controlled clinical studies, infants in the Exosurf Neonatal group showed significant improvements in FiO_2 and ventilator settings which persisted for at least 7 days. Pulmonary air leaks were significantly reduced in each study. Five of these studies also showed a significant reduction in death from RDS. Further, overall mortality was reduced for all infants weighing >700 grams. The one versus three-dose prophylactic treatment study in 700 to 1100 gram infants showed a further reduction in overall mortality with two additional doses.

Safety information is presented in Tables 3 and 4 (see ADVERSE REACTIONS). Beneficial effects in the Exosurf Neonatal group were observed for some safety assessments. Various forms of pulmonary air leak and use of pancuronium were reduced in infants receiving Exosurf Neonatal in all six studies.

Follow-up data at one year adjusted age are available on 1094 of 2470 surviving infants. Growth and development of infants who received Exosurf Neonatal in this sample were comparable to infants who received placebo.

INDICATIONS AND USAGE: Exosurf Neonatal is indicated for:

1. **Prophylactic** treatment of infants with birth weights of less than 1350 grams who are at risk of developing RDS (see PRECAUTIONS),
2. **Prophylactic** treatment of infants with birth weights greater than 1350 grams who have evidence of pulmonary immaturity, and
3. **Rescue** treatment of infants who have developed RDS.

For **prophylactic** treatment, the first dose of Exosurf Neonatal should be administered as soon as possible after birth (see DOSAGE AND ADMINISTRATION: General Guidelines for Administration).

Infants considered as candidates for **rescue** treatment with Exosurf Neonatal should be on mechanical ventilation and have a diagnosis of RDS by both of the following criteria:

1. Respiratory distress not attributable to causes other than RDS, based on clinical and laboratory assessments.
2. Chest radiographic findings consistent with the diagnosis of RDS.

During the clinical development of Exosurf Neonatal, all infants who received the drug were intubated and on mechanical ventilation. For three-dose prophylactic treatment with Exosurf Neonatal, the first dose of drug was administered as soon as possible after birth and repeat doses were given at approximately 12 and 24 hours after birth if infants remained on mechanical ventilation at those times. For rescue treatment, two doses were given; one between 2 and 24 hours of life, and a second approximately 12 hours later if infants remained on mechanical ventilation. Infants who received rescue treatment with Exosurf Neonatal had a documented arterial to alveolar oxygen tension ratio (a/A) <0.22.

CONTRAINDICATIONS: There are no known contraindications to treatment with Exosurf Neonatal.

WARNINGS:

Intratracheal Administration Only: Exosurf Neonatal should be administered only by instillation into the trachea (see DOSAGE AND ADMINISTRATION).

General:

The use of Exosurf Neonatal requires expert clinical care by experienced neonatologists and other clinicians who are accomplished at neonatal intubation and ventilatory management. Adequate personnel, facilities, equipment, and medications are required to optimize perinatal outcome in premature infants.

Instillation of Exosurf Neonatal should be performed **only** by trained medical personnel experienced in airway and clinical management of unstable premature infants. Vigilant clinical attention should be given to all infants prior to, during, and after administration of Exosurf Neonatal.

Acute Effects: Exosurf Neonatal can rapidly affect oxygenation and lung compliance.

Lung Compliance: If chest expansion improves substantially after dosing, peak ventilator inspiratory pressures should be reduced immediately, without waiting for confirmation of respiratory improvement by blood gas assessment. Failure to reduce inspiratory ventilator pressures rapidly in such instances can result in lung overdistention and fatal pulmonary air leak.

Hyperoxia: If the infant becomes pink and transcutaneous oxygen saturation is in excess of 95%, FiO_2 should be reduced in small but repeated steps (until saturation is 90 to 95%) without waiting for confirmation of elevated arterial pO_2 by blood gas assessment. Failure to reduce FiO_2 in such instances can result in hyperoxia.

Hypocarbia: If arterial or transcutaneous CO_2 measurements are <30 torr, the ventilator rate should be reduced at once. Failure to reduce ventilator rates in such instances can result in marked hypocarbia, which is known to reduce brain blood flow.

Pulmonary Hemorrhage: In the single study conducted in infants weighing <700 grams at birth, the incidence of pulmonary hemorrhage (10% vs 2% in the placebo group) was significantly increased in the Exosurf Neonatal group. None of the five studies involving infants with birth weights >700 grams showed a significant increase in pulmonary hemorrhage in the Exosurf Neonatal group. In a cross-study analysis of these five studies, pulmonary hemorrhage was reported for 1% (14/1420) of infants in the placebo group and 2% (27/1411) of infants in the Exosurf Neonatal group. Fatal pulmonary hemorrhage occurred in three infants; two in the Exosurf Neonatal group and one in the placebo group. Mortality from all causes among infants who developed pulmonary hemorrhage was 43% in the placebo group and 37% in the Exosurf Neonatal group.

Pulmonary hemorrhage in both Exosurf Neonatal and placebo infants was more frequent in infants who were younger, smaller, male, or who had a patent ductus arteriosus. Pulmonary hemorrhage typically occurred in the first 2 days of life in both treatment groups.

In more than 7700 infants in the open, uncontrolled study, pulmonary hemorrhage was reported in 4%, but fatal pulmonary hemorrhage was reported rarely (0.4%).

In the controlled clinical studies, Exosurf Neonatal treated infants who received steroids more than 24 hours prior to delivery or indomethacin postnatally had a lower rate of pulmonary hemorrhage than other Exosurf Neonatal treated infants. Attention should be paid to early and aggressive diagnosis and treatment (unless contraindicated) of patent ductus arteriosus during the first 2 days of life (while the ductus arteriosus is often clinically silent). Other potentially protective measures include attempting to decrease FiO_2 preferentially over ventilator pressures during the first 24 to 48 hours after dosing, and attempting to decrease PEEP minimally for at least 48 hours after dosing.

Mucous Plugs: Infants whose ventilation becomes markedly impaired during or shortly after dosing may have mucous plugging of the endotracheal tube, particularly if pulmonary secretions were prominent prior to drug administration. Suctioning of all infants prior to dosing may lessen the chance of mucous plugs obstructing the endotracheal tube. If endotracheal tube obstruction from such plugs is suspected, and suctioning is unsuccessful in removing the obstruction, the blocked endotracheal tube should be replaced immediately.

PRECAUTIONS:

General: In the controlled clinical studies, infants known prenatally or postnatally to have major congenital anomalies, or who were suspected of having congenital infection, were excluded from entry. However, these disorders cannot be recognized early in life in all cases, and a few infants with these conditions were entered. The benefits of Exosurf Neonatal in the affected infants who received drug appeared to be similar to the benefits observed in infants without anomalies or occult infection.

Prophylactic Treatment–Infants <700 Grams: In infants weighing 500 to 700 grams, a single prophylactic dose of Exosurf Neonatal significantly: improved FiO_2 and ventilator settings, reduced pneumothorax, and reduced death from RDS, but increased pulmonary hemorrhage (see WARNINGS). Overall mortality did not differ significantly between the placebo and Exosurf Neonatal groups (see Table 1). Data on multiple doses in infants in this weight class are not yet available. Accordingly, clinicians should carefully evaluate the potential risks and benefits of Exosurf Neonatal administration in these infants.

Rescue Treatment–Number of Doses: A small number of infants with RDS have received more than two doses of Exosurf Neonatal as rescue treatment. Definitive data on the safety and efficacy of these additional doses are not available.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Exosurf Neonatal at concentrations up to 10,000 μg/plate was not mutagenic in the Ames Salmonella assay.

Long-term studies have not been performed in animals to evaluate the carcinogenic potential of Exosurf Neonatal.

The effects of Exosurf Neonatal on fertility have not been studied.

ADVERSE REACTIONS:

General: Premature birth is associated with a high incidence of morbidity and mortality. Despite significant reductions in overall mortality associated with Exosurf Neonatal, some infants who received Exosurf Neonatal developed severe complications and either survived with permanent handicaps or died.

In controlled clinical studies evaluating the safety and efficacy of Exosurf Neonatal, numerous safety assessments were made. In infants receiving Exosurf Neonatal, pulmonary hemorrhage, apnea and use of methylxanthines were increased. A number of other adverse events were significantly reduced in the Exosurf Neonatal group, particularly various forms of pulmonary air leak and use of pancuronium. (See CLINICAL PHARMACOLOGY: Clinical Results.) Tables 3 and 4 summarize the results of the major safety evaluations from the controlled clinical studies.

Circle 118 on reader service card

Table 3 **Safety Assessments[a]—Prophylactic Treatment**

Number of Doses:	Single Dose		Single Dose		Single Dose		One Versus Three Doses	
Birth Weight Range:	500 to 700 grams		700 to 1350 grams		700 to 1100 grams		700 to 1100 grams	
Treatment Group:	Placebo (Air)	EXOSURF	Placebo (Air)	EXOSURF	Placebo (Air)	EXOSURF	One EXOSURF Dose	Three EXOSURF Doses
Number of Infants:	N=108	N=107	N=193	N=192	N=222	N=224	N=356	N=360
	% of Infants		% of Infants		% of Infants		% of Infants	
Intraventricular Hemorrhage (IVH)								
Overall	51	57	31	27	36	36	38	35
Severe IVH	26	25	10	8	13	14	9	9
Pulmonary Air Leak (PAL)								
Overall	52	48	16	11	32	25	29	27
Pneumothorax	23	10*	5	6	19	11*	14	12
Pneumopericardium	1	4	2	0	<1	1	1	1
Pneumomediastinum	2	1	2	3	7	1**	3	2
Pulmonary Interstitial Emphysema	43	44	13	7*	26	20	23	22
Death from PAL	4	6	<1	<1	2	1	2	1
Patent Ductus Arteriosus	49	53	66	70	50	55	59	57
Necrotizing Enterocolitis	2	4	11	13	3	4	6	2*
Pulmonary Hemorrhage	2	10**	2	4	1	4	4	6
Congenital Pneumonia	4	4	2	4	2	2	1	1
Nosocomial Pneumonia	10	10	2	4	4	7	14	15
Non-Pulmonary Infections	33	35	34	39	28	29	35	34
Sepsis	30	34	30	34	23	24	30	27
Death From Sepsis	4	4	3	3	1	2	3	2
Meningitis	4	6	3	1	2	3	1	2
Other Infections	7	4	5	3	6	10	10	11
Major Anomalies	3	1	2	4	7	4	4	4
Hypotension	70	77	52	47	59	62	54	50
Hyperbilirubinemia	22	21	63	61	27	31	20	21
Exchange Transfusion	4	3	1	2	2	2	3	1
Thrombocytopenia[b]	21	25	not available		9	8	12	10
Persistent Fetal Circulation	0	1	1	1	0	2*	1	<1
Seizures	11	8	2	2	11	9	6	5
Apnea	34	33	76	73	55	65*	62	68
Drug Therapy								
Antibiotics	96	99	98	96	98	99	>99	99
Diuretics	55	60	39	37	59	63	64	65
Anticonvulsants	14	18	23	24	20	16	9	8
Inotropes	46	40	20	20	26	20	28	27
Sedatives	62	71	65	64	63	57	52	52
Pancuronium	19	11	22	14*	19	13*	15	11
Methylxanthines	38	43	77	77	61	72*	75	82*

[a] All parameters were examined with "as-treated" analyses.
[b] Thrombocytopenia requiring platelet transfusion.
* $p<0.05$
** $p<0.01$

Table 4 **Safety Assessments[a]—Rescue Treatment**

Number of Doses:	Two Doses		Two Doses	
Birth Weight Range:	700 to 1350 grams		1250 grams and above	
Treatment Group:	Placebo (Air)	EXOSURF	Placebo (Air)	EXOSURF
Number of Infants:	N=213	N=206	N=622	N=615
	% of Infants		% of Infants	
Intraventricular Hemorrhage (IVH)				
Overall	48	52	23	18*
Severe IVH	13	9	5	4
Pulmonary Air Leak (PAL)				
Overall	54	34***	30	18***
Pneumothorax	29	20*	20	10***
Pneumopericardium	4	1	1	2
Pneumomediastinum	8	4	5	2**
Pulmonary Interstitial Emphysema	48	25***	24	13***
Death from PAL	7	3	<1	1
Patent Ductus Arteriosus	66	57	54	45*
Necrotizing Enterocolitis	3	3	1	2
Pulmonary Hemorrhage	3	1	<1	1
Congenital Pneumonia	2	3	2	2
Nosocomial Pneumonia	5	7	2	2
Non-Pulmonary Infections	19	22	13	13
Sepsis	15	17	8	8
Death From Sepsis	<1	<1	1	<1
Meningitis	1	<1	1	<1*
Other Infections	5	8	5	6
Major Anomalies	3	3	4	4
Hypotension	62	57	50	39**
Hyperbilirubinemia	17	19	12	10
Exchange Transfusion	3	4	1	2
Thrombocytopenia[b]	10	11	4	<1**
Persistent Fetal Circulation	1	1	6	2**
Seizures	10	10	6	3*
Apnea	48	65**	37	44*
Drug Therapy				
Antibiotics	100	99	98	98
Diuretics	60	65	45	34***
Anticonvulsants	17	17	10	5**
Inotropes	36	31	27	16***
Sedatives	72	68	76	64***
Pancuronium	34	17**	33	15***
Methylxanthines	62	74**	49	53

[a] All parameters were examined with "as-treated" analyses.
[b] Thrombocytopenia requiring platelet transfusion.
* $p<0.05$
** $p<0.01$
*** $p<0.001$

Pulmonary Hemorrhage: See WARNINGS.

Abnormal Laboratory Values: Abnormal laboratory values are common in critically ill, mechanically ventilated, premature infants. A higher incidence of abnormal laboratory values in the Exosurf Neonatal group was not reported.

Events During Dosing: Data on events during dosing are available from more than 8800 infants in the open, uncontrolled clinical study (Table 5).

Table 5 **Events During Dosing in the Open, Uncontrolled Study[a]**

Treatment Type:	Prophylactic Treatment	Rescue Treatment
Number of Infants:	N=1127	N=7711
	% of Infants	% of Infants
Reflux of Exosurf	20	31
Drop in O_2 saturation ($\geq$20%)	6	22
Rise in O_2 saturation ($\geq$10%)	5	6
Drop in transcutaneous pO_2 ($\geq$20 mm Hg)	1	8
Rise in transcutaneous pO_2 ($\geq$20 mm Hg)	2	5
Drop in transcutaneous pCO_2 ($\geq$20 mm Hg)	<1	1
Rise in transcutaneous pCO_2 ($\geq$20 mm Hg)	1	3
Bradycardia (<60 beats/min)	1	3
Tachycardia (>200 beats/min)	<1	<1
Gagging	1	5
Mucous Plugs	<1	<1

[a] Infants may have experienced more than one event.
Investigators were prohibited from adjusting FiO_2 and/or ventilator settings during dosing unless significant clinical deterioration occurred.

Reflux: Reflux of Exosurf Neonatal into the endotracheal tube during dosing has been observed and may be associated with rapid drug administration. If reflux occurs, drug administration should be halted and, if necessary, peak inspiratory pressure on the ventilator should be increased by 4 to 5 cm H_2O until the endotracheal tube clears.

>20% Drop in Transcutaneous Oxygen Saturation: If transcutaneous oxygen saturation declines during dosing, drug administration should be halted and, if necessary, peak inspiratory pressure on the ventilator should be increased by 4 to 5 cm H_2O for 1 to 2 minutes. In addition, increases of FiO_2 may be required for 1 to 2 minutes.

Mucous Plugs: See WARNINGS.

OVERDOSAGE: There have been no reports of massive overdosage with Exosurf Neonatal.

DOSAGE AND ADMINISTRATION:

Preparation of Suspension: Exosurf Neonatal is best reconstituted immediately before use because it does not contain antibacterial preservatives. However, the reconstituted suspension is chemically and physically stable when stored at 2° to 30°C (36° to 86°F) for up to 12 hours following reconstitution.

Solutions containing buffers or preservatives should not be used for reconstitution. **Do Not Use Bacteriostatic Water for Injection, USP.** Each vial of Exosurf Neonatal should be reconstituted only with **8 mL** of the accompanying diluent (preservative-free Sterile Water for Injection) as follows: **1.** Fill a 10 mL or 12 mL syringe with 8 mL preservative-free Sterile Water for Injection using an 18 or 19 gauge needle; **2.** Allow the vacuum in the vial to draw the sterile water into the vial; **3.** Aspirate as much as possible of the 8 mL out of the vial into the syringe (while maintaining the vacuum), then SUDDENLY release the syringe plunger.

Step 3 should be repeated three or four times to assure adequate mixing of the vial contents. If vacuum is not present, the vial of Exosurf Neonatal should not be used.

The appropriate dosage volume for the entire dose (5 mL/kg) should then be drawn into the syringe from **below** the froth in the vial (again maintaining the vacuum). If the infant weighs less than 1600 grams, unused Exosurf Neonatal suspension will remain in the vial after the entire dose is drawn into the syringe. If the infant weighs more than 1600 grams, at least two vials will be required for each dose.

Reconstituted Exosurf Neonatal is a milky white suspension with a total volume of 8 mL per vial. Each mL of reconstituted Exosurf Neonatal contains 13.5 mg colfosceril palmitate, 1.5 mg cetyl alcohol, 1 mg tyloxapol, and sodium chloride to provide a 0.1 N concentration. If the suspension appears to separate, gently shake or swirl the vial to resuspend the preparation. The reconstituted product should be inspected visually for homogeneity immediately before administration; if persistent large flakes or particulates are present, the vial should not be used.

Dosage: Accurate determination of weight at birth is the key to accurate dosing.

Prophylactic Treatment: The first dose of Exosurf Neonatal should be administered as a single 5 mL/kg dose as soon as possible after birth. Second and third doses should be administered approximately 12 and 24 hours later to all infants who remain on mechanical ventilation at those times.

Rescue Treatment: Exosurf Neonatal should be administered in two 5 mL/kg doses. The initial dose should be administered as soon as possible after the diagnosis of RDS is confirmed. The second dose should be administered approximately 12 hours following the first dose, provided the infant remains on mechanical ventilation. A small number of infants with RDS have received more than two doses of Exosurf Neonatal as rescue treatment. Definitive data on the safety and efficacy of these additional doses are not available (see PRECAUTIONS).

Use of Special Endotracheal Tube Adapter: With each vial of Exosurf Neonatal Intratracheal Suspension, five different sized endotracheal tube adapters each with a special right angle Luer®-lock sideport are supplied. The adapters are clean but not sterile. The adapters should be used as follows: **1.** Select an adapter size which corresponds to the inside diameter of the endotracheal tube. **2.** Insert the adapter into the endotracheal tube with a firm push-twist motion. **3.** Connect the breathing circuit wye to the adapter. **4.** Remove the cap from the sideport on the adapter. Attach the syringe containing drug to the sideport. **5.** After completion of dosing, remove the syringe and RECAP THE SIDEPORT.

Administration: The infant should be suctioned prior to administration of Exosurf Neonatal.

Exosurf Neonatal suspension is administered via the sideport on the special endotracheal tube adapter **WITHOUT INTERRUPTING MECHANICAL VENTILATION.**

Each Exosurf Neonatal dose is administered in two 2.5 mL/kg half-doses. Each half-dose is instilled slowly over 1 to 2 minutes (30 to 50 mechanical breaths) in small bursts timed with inspiration. After the first 2.5 mL/kg half-dose is administered in the midline position, the infant's head and torso are turned 45° to the **right** for 30 seconds while mechanical ventilation is continued. After the infant is returned to the midline position, the second 2.5 mL/kg half-dose is given in an identical fashion over another 1 to 2 minutes. The infant's head and torso are then turned 45° to the **left** for 30 seconds while mechanical ventilation is continued, and the infant is then turned back to the midline position. These maneuvers allow gravity to assist in the distribution of Exosurf Neonatal in the lungs.

During dosing, heart rate, color, chest expansion, facial expressions, the oximeter, and the endotracheal tube patency and position should be monitored. If heart rate slows, the infant becomes dusky or agitated, transcutaneous oxygen saturation falls more than 15%, or Exosurf Neonatal backs up in the endotracheal tube, dosing should be slowed or halted and, if necessary, the peak inspiratory pressure, ventilator rate, and/or FiO_2 turned up. On the other hand, rapid improvements in lung function may require immediate reductions in peak inspiratory pressure, ventilator rate, and/or FiO_2. (See WARNINGS and see below for additional information concerning administration.)

Suctioning should not be performed for two hours after Exosurf Neonatal is administered, except when dictated by clinical necessity.

General Guidelines for Administration: Administration of Exosurf Neonatal should not take precedence over clinical assessment and stabilization of critically ill infants.

Intubation: Prior to dosing with Exosurf Neonatal, it is important to ensure that the endotracheal tube tip is in the trachea and not in the esophagus or right or left mainstem bronchus. Brisk and symmetrical chest movement with each mechanical inspiration should be confirmed prior to dosing, as should equal breath sounds in the two axillae. In prophylactic treatment, dosing with Exosurf Neonatal need not be delayed for radiographic confirmation of the endotracheal tube tip position. In rescue treatment, bedside confirmation of endotracheal tube tip position is usually sufficient, if at least one chest radiograph subsequent to the last intubation confirmed proper position of the endotracheal tube tip. Some lung areas will remain undosed if the endotracheal tube tip is too low.

Monitoring: Continuous ECG and transcutaneous oxygen saturation monitoring during dosing are essential. In most infants treated prophylactically, it should be possible to initiate such monitoring prior to administration of the first dose of Exosurf Neonatal. For subsequent prophylactic and all rescue doses, arterial blood pressure monitoring during dosing is also highly desirable. After both prophylactic and rescue dosing, frequent arterial blood gas sampling is required to prevent post-dosing hyperoxia and hypocarbia (see WARNINGS).

Ventilatory Support During Dosing: The 5 mL/kg dosage volume may cause transient impairment of gas exchange by physical blockage of the airway, particularly in infants on low ventilator settings. As a result, infants may exhibit a drop in oxygen saturation during dosing, especially if they are on low ventilator settings prior to dosing. These transient effects are easily overcome by increasing peak inspiratory pressure on the ventilator by 4 to 5 cm H_2O for 1 to 2 minutes during dosing. FiO_2 can also be increased if necessary. In infants who are particularly fragile or reactive to external stimuli, increasing peak inspiratory pressure by 4 to 5 cm H_2O and/or FiO_2 20% just prior to dosing may minimize any transient deterioration in oxygenation. However, in virtually all cases it should be possible to return the infant to pre-dose settings within a very short time of dose completion.

Post-Dosing: At the end of dosing, position of the endotracheal tube should be confirmed by listening for equal breath sounds in the two axillae. Attention should be paid to chest expansion, color, transcutaneous saturation, and arterial blood gases. Some infants who receive Exosurf Neonatal and other surfactants respond with rapid improvements in pulmonary compliance, minute ventilation, and gas exchange (see WARNINGS). Constant bedside attention of an experienced clinician for at least 30 minutes after dosing is essential. Frequent blood gas sampling also is absolutely essential. Rapid changes in lung function require immediate changes in peak inspiratory pressure, ventilator rate, and/or FiO_2.

HOW SUPPLIED: Exosurf Neonatal for Intratracheal Suspension is supplied in a carton containing one 10 mL vial of Exosurf Neonatal for Intratracheal Suspension, one 10 mL vial of Sterile Water for Injection, and five endotracheal tube adapters (2.5, 3.0, 3.5, 4.0, and 4.5 mm). (NDC 0081-0207-01)

Store Exosurf Neonatal for Intratracheal Suspension at 15° to 30°C (59° to 86°F) in a dry place.

EDUCATIONAL MATERIAL: A videotape on dosing is available from your Burroughs Wellcome Co. representative. This videotape demonstrates techniques for safe administration of Exosurf Neonatal and should be viewed by health care professionals who will administer the drug.

Licensed under U.S. Patent Nos. 4312860 and 4826821

BURROUGHS WELLCOME CO., Research Triangle Park, NC 27709
Printed in U.S.A. August 1990

Portable Airway-Suction Systems: A Comparison of Performance

John F Curran RRT, Kevin S Stanek BSEE, and Robert M Kacmarek PhD RRT

A number of portable suction systems (powered either manually, pneumatically, or electrically) are available. We compared the performance of three electric systems (Laerdal Medical LSU, Laerdal Medical CSU, and Matrx Medical) and two manual systems (Vitalograph Emergency Aspirator and California Medical V-VAC) to wall suction set at maximum pressure of 300 torr [39.9 kPa]. METHODS: We determined the maximum pressure each system was capable of generating, and we measured the volume of imitation maple syrup each system at maximum pressure could suction within 5 seconds and the time required by each system at maximum pressure to suction 150 mL of syrup. In addition, we evaluated the life of each electric system's internal battery. RESULTS: All the electric systems were capable of generating suction pressure > 300 torr [39.9 kPa]. The amount of time required by the electric systems to suction 150 mL of syrup was not significantly different from that required by wall suction. In 5 seconds, wall suction suctioned a significantly greater volume of syrup than did the Matrx Medical system ($p < 0.05$, ANOVA), but a significantly smaller volume of syrup than did the Laerdal Medical CSU system ($p < 0.05$, ANOVA). The manual Vitalograph Emergency Aspirator was capable of generating 300 torr [39.9 kPa] pressure, but the California Medical V-VAC was not. Wall suction significantly outperformed both of the manual systems when volume of syrup suctioned in 5 seconds and time required to suction 150 mL of syrup were compared ($p < 0.05$ ANOVA). All electric systems were capable of maintaining maximum suction > 15 minutes. CONCLUSIONS: Although statistically significant differences in performance were observed between the portable systems and wall suction, all portable systems exceeded performances required clinically. Even the California Medical V-VAC system, whose performance least resembled that of wall suction, proved capable of generating a maximum pressure exceeding the standard suction pressure (120-150 torr [16.0-20.0 kPa]) used in adults. However, of concern is the fact that none of these portable systems have pressure regulators, and all except the California Medical V-VAC are capable of generating dangerously high suction pressures. (Respir Care 1991;36:259-266.)

Introduction

Oropharyngeal and tracheal suctioning is essential for appropriate airway care and resuscitation procedures.[1,2] Although most hospital patient-rooms today have wall suction, many locations where emergency airway care and resuscitation may be required do not have wall suction. Even in the most modern of hospitals, wall suction is not commonly available in waiting rooms, cafeterias, and some laboratories. Numerous portable suction systems are currently manufactured for use in hospitals, home-care settings, and in the field. These systems are powered either manually, pneumatically, or electrically (with internal rechargeable batteries).

We evaluated the performance of three electric systems (Laerdal Medical LSU [Fig. 1], Laerdal Medical CSU [Fig. 2], and Matrx Medical [Fig.

Mr Curran is a Staff Therapist, Respiratory Care Services, and Mr Stanek is a Clinical Engineer, Department of Anesthesiology, Massachusetts General Hospital; and Dr Kacmarek is Assistant Professor, Department of Anesthesiology, Harvard Medical School, and Director, Respiratory Care Services, Massachusetts General Hospital—Boston, Massachusetts.

A version of this paper was presented by Mr Curran at the Respiratory Care Open Forum during the 1990 AARC Annual Meeting in New Orleans, Louisiana.

Reprints: Robert M Kacmarek PhD RRT, Respiratory Care, Ellison-4, Massachusetts General Hospital, Boston MA 02114.

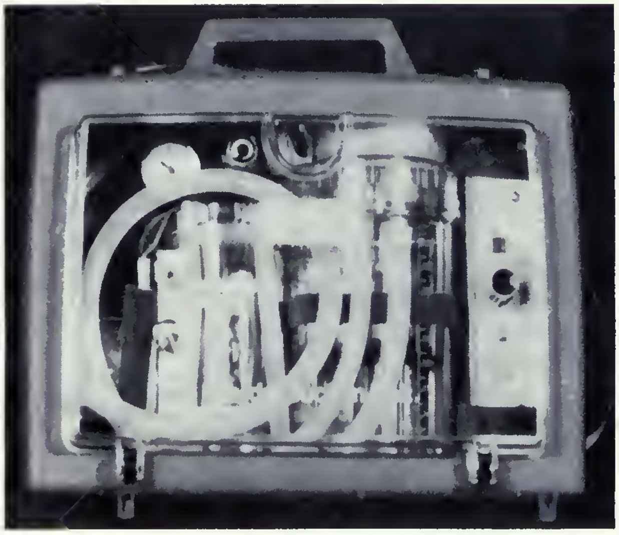


Fig. 1. Laerdal Medical LSU portable suction system.

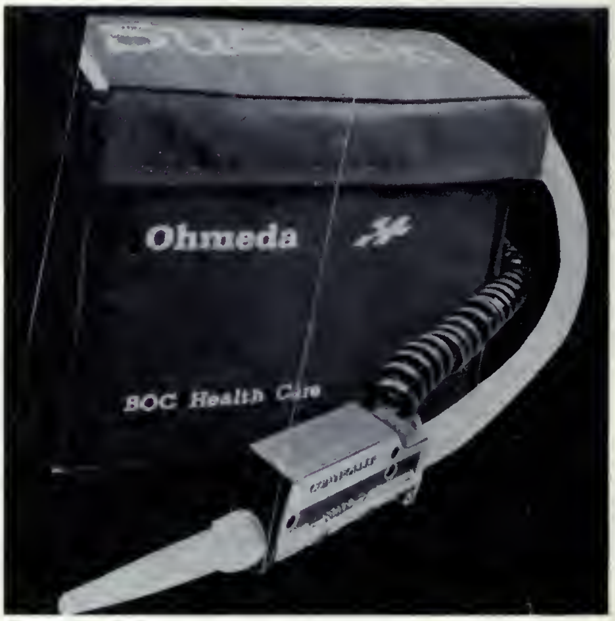


Fig. 3. Matrx Medical portable suction system. (This product line was recently acquired from Ohmeda.)

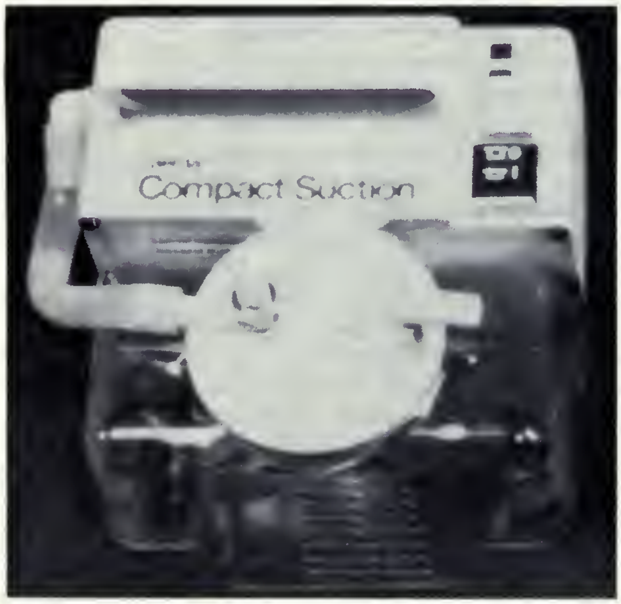


Fig. 2. Laerdal Medical CSU portable suction system.

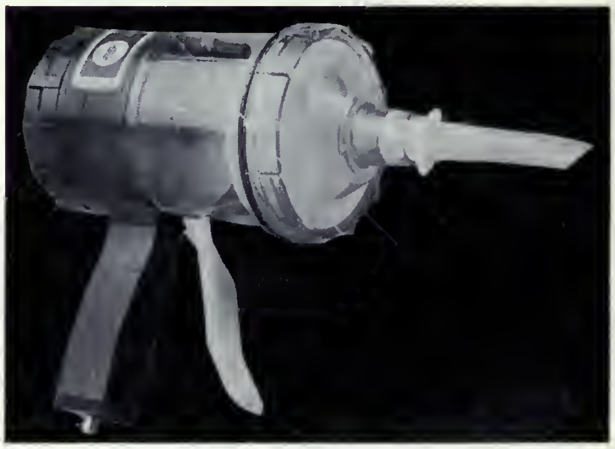


Fig. 4. Vitalograph Emergency Aspirator portable suction system.

3]) and two manual systems (Vitalograph Emergency Aspirator [Fig. 4], and California Medical V-VAC [Fig. 5]).

Materials and Methods

We compared the maximal performance of five portable suction systems to that of wall suction set at 300 torr [39.9 kPa], by measuring: (1) maximum suction pressure generated after complete obstruction of the suction line; (2) volume of a viscous fluid (imitation maple syrup, Stop & Save brand) suctioned within 5 seconds; and (3) amount of time required to suction 150 mL of the viscous fluid. In addition, the battery life of each of the three electric systems was evaluated, and the operational variance of the V-VAC was determined at its High, Medium, and Low settings.

To determine the maximal pressure each system was capable of generating, each system was operated

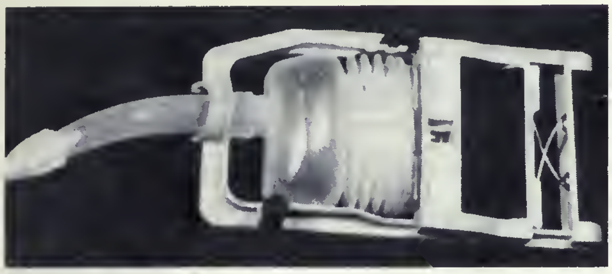


Fig. 5. California Medical Products V-VAC portable suction system.

at its highest suction setting with the suction tubing or port completely occluded. (The California Medical V-VAC was evaluated at its High, Medium, and Low settings.) Pressure was monitored immediately proximal to the point of occlusion by a calibrated Validyne pressure transducer (MP45-32-871, ±880 cm H_2O), and recorded by a Hewlett-Packard System 7758-B strip-chart recorder (Fig. 6). During evaluation of the electric suction systems, a standard 5-foot length of plastic tubing (1/2-inch external diameter) separated the system from the pressure-transducer connector. During evaluation of the manual systems, the pressure transducer was attached directly to the suction system. During evaluation of wall suction, a 5-foot length of Tygon tubing separated the fluid-collection chamber from the transducer connector. The setup for each system was chosen to simulate the way it is actually used. Each system was tested with the collection chamber filled with water to one half its capacity and with it empty. Under each condition, five trials of sustained suction (15-second duration) were recorded for wall suction and the electric systems, and five manual generations of suction were recorded for the hand-operated systems.

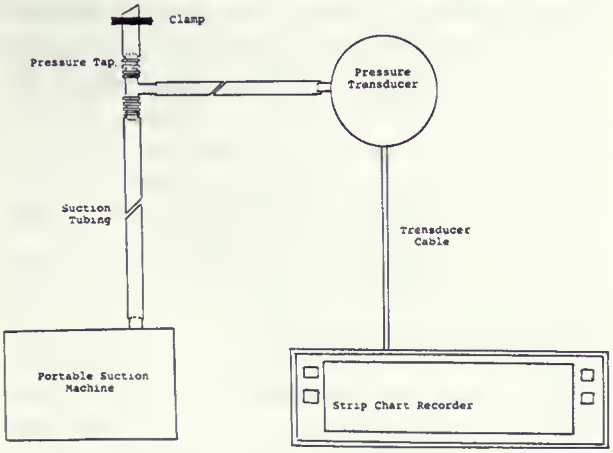


Fig. 6. Illustration of setup used to measure pressures generated by the portable suction systems. See text for details.

During evaluations of the volume of viscous fluid suctioned within 5 seconds and the time required to suction 150 mL of viscous fluid, a 14-Fr Yankauer (tonsil-tip) tube was attached to the tygon tubing connected to the electric systems and the wall-suction collection chamber, and directly to the manual systems. Imitation maple syrup was the viscous fluid used in both of these evaluations. Prior to each of these evaluations, syrup was placed in a graduated cylinder to a level of 150 mL. During the 5-second evaluation, we compared the Before and After volume of syrup in the cylinder. Prior to evaluation of the time required to suction 150 mL of syrup, each respective suction system was emptied. During these two evaluations, the electric suction systems were run by alternating current rather than by internal battery. Five trials of each evaluation were performed for each suction system.

The battery life of each electric suction system was evaluated by determining the length of suction time required for a 25% reduction in maximum suction pressure to occur. The setup for measurement was the same used during the evaluation of maximum suction (Fig. 6). During evaluation, each suction system was run for 30 seconds with the tubing clamped; following this, the system was shut off for 15 seconds, and then run again for 30 seconds. This was repeated until a 25% reduction in maximum pressure was observed. Prior to this evaluation, each suction system was charged for at least 24 hours. Only one trial was performed on each system.

Description of Suction Systems

A comparison of the functional capabilities and prices of the five systems evaluated is provided in Table 1. All of the electric systems operate essentially the same, each with a battery. The Laerdal Medical CSU is the smallest of the three. The two manual systems, although they operate similarly, differ: the V-VAC consists of a nondisposable frame and a disposable chamber; and the Vitalograph contains a one-way valve, which

Table 1. Comparison of Functional Capabilities and Prices of Portable Suction Systems Evaluated

System	Vacuum Settings	Fluid-Container Capacity	Size	List Price
Laerdal LSU	Maximum and ½ of maximum	1000 mL	10.5 lbs 12.5" × 14" × 5.2"	$520
Laerdal CSU	Continuous variation maximum to zero	1000 mL	2.5 lbs 6.5" × 6.0" × 4.5"	$395
Matrx Medical	Maximum only	1200 mL	6.5 lbs 11.5" × 11" × 5"	$470
Vitalograph Emergency Aspirator	Variable with force and frequency of manual compression: A pressure plateau is obtainable.	240 mL	1.44 lbs 8.4" × 4.0" × 9.2"	$140
California Medical V-VAC	Hi, Medium, and Low settings—Affected by force of compression. Pressure drops to zero between compressions.	425 mL	1.0 lb 15.7" × 2.8" × 5.2"	$ 70

allows maintenance of a pressure plateau, while the V-VAC returns to zero in between compressions (even if the inlet is completely occluded).

Statistical Analysis

One-way analysis of variance (ANOVA) was used to determine the significance of differences between each suction system and wall suction for maximum pressure, volume of syrup suctioned in 5 seconds, and amount of time required to suction 150 mL of syrup. Significance was set at $p < 0.05$.

Results

Tables 2 through 4 list the results of the various comparisons for all systems evaluated. The maximum suction pressure generated by each of the electric systems (empty or half full) was significantly greater than 300 torr [39.9 kPa] ($p < 0.05$). The maximum pressure generated by the V-VAC was significantly less than 300 torr [39.9 kPa] ($p < 0.05$).

The volume of syrup suctioned in 5 seconds by the Laerdal Medical CSU was significantly greater than that suctioned by wall suction ($p < 0.05$), while the volumes suctioned by the Matrx, Vitalograph, and V-VAC systems were significantly less than that suctioned by wall suction ($p < 0.05$).

The times required by the electric systems to suction 150 mL of syrup were not significantly different from the time required by wall suction ($p < 0.05$); whereas, the times required by the manual systems were significantly greater than that required by wall suction ($p < 0.05$). Use of the V-VAC to suction was discontinued after 2 minutes of continual manual compression; mean (SD) volume of 100 (7.3) mL of syrup was suctioned during this 2-min period. The function of both manual systems is dependent on user strength and stamina; however, with both systems, effort during the five trials was consistent (standard deviation of volume suctioned was 3.8 mL using the Vitalograph and 7.3 mL using the V-VAC).

The internal battery life of all electric systems exceeded 15 minutes (Table 3) before a 25%

Table 2. Performance Comparison: Portable Suction Systems vs Wall Suction

Suction Systems	Maximum Pressure* reservoir empty	Maximum Pressure* reservoir ½ full	Volume Suctioned[†] in seconds	Suction Time[‡] for 150 mL
Wall Suction	300	300	33.2 (3.6)	51.6 (6.9)
Laerdal Medical LSU	517 (3.5)[§]	514 (4.2)[§]	24.4 (9.5)	56.6 (3.1)
Laerdal Medical CSU	515 (3.5)[§]	514 (2.5)[§]	42.8 (4.1)[§]	42.8 (2.3)
Matrx Medical Inc	466 (5.7)[§]	452 (4.8)[§]	16.0 (4.9)[§]	50 (1.1)
Vitalograph Emergency	283 (15.7)	304 (24)	20.0 (9.9)[§]	63.0 (3.8)[§]
California Medical V-VAC	193 (9.4)[§]	217 (8.1)[§]	9.2 (1.8)[§]	120[§] [‖]

All values are mean (SD) of 5 trials.

* Maximum pressure (in torr) generated during complete occlusion.

[†] Volume of syrup (in mL) suctioned in a 5-second period.

[‡] Time required (in seconds) to suction 150 mL of syrup.

[§] Significantly different from wall suction ($p < 0.05$ ANOVA).

[‖] Stopped after 2 minutes of suctioning, mean (SD) volume of syrup suctioned was 100 (7.3) mL.

reduction in maximum pressure occurred. Greater than 75% of maximum pressure could be generated by the Laerdal CSU for 33 minutes, by the Laerdal LSU for 27 minutes, and by the Matrx for 17.5 minutes; but pressure dropped to zero more gradually with the LSU (6 minutes) and Matrx (5 minutes) than with the CSU (3 minutes).

Evaluation of the V-VAC at various settings produced predictable results. With the V-VAC system empty and half full, maximum pressure decreased as the suction setting was moved from High to Medium to Low. When the system was half full, pressures were slightly higher than when the system was empty.

Table 3. Performance Comparisons: Internal Battery Life of Portable Electric Suction Systems

Suction System	Initial Pressure (torr)	Final Pressure (torr)	Total Time to Final Pressure (min)
Laerdal Medical LSU	520	360	27
Laerdal Medical CSU	560	308	33
Matrx Medical	480	280	17.5

Discussion

Each of the systems evaluated was capable of equaling the 300-torr [39.9-kPa] wall suction we used as a standard except the V-VAC, which was only capable of generating a mean (SD) maximum pressure of 193 (9.4) torr [25.7 (1.3) kPa]. In fact, the three electric systems could generate pressures exceeding 450 torr [59.9 kPa]. However, are these high suction levels necessary or, for that matter, safe?

In 1956, Plum and Dunning[3] first documented the adverse effects of suctioning on the tracheobronchial tree. They examined the excised trachea

Table 4. Maximum Pressure Generated by the California Medical V-VAC at 3 Suction Settings*

Setting	Reservoir Empty	Reservoir ½ Full of H_2O
High	193 (9.4)	217.5 (8.1)
Medium	150 (6.2)	157.5 (3.8)
Low	82 (3.8)	90 (4.8)

---

*All pressures are in torr and mean (SD).

and main-stem bronchi of eight patients during autopsy, all of whom had had tracheostomies and had been regularly suctioned with vacuum pressure ranging from 250-380 torr [33.3-50.5 kPa]. In all airways examined, the trachea was grossly hemorrhagic and edematous. The surface of the mucous membrane was lusterless and covered with a moderate amount of hemorrhagic exudate. In five of the eight airways examined, ulcers were also noted on the tracheal wall.

Similar results were noted by Thambiran and Ripley[4] in 1966 when they studied the effects of 50-300 torr [6.7-39.9 kPa] of suction on the airways of six kittens. As pressure was increased, damage to the airway increased. Even in the kitten suctioned at 50 torr [6.7 kPa], epithelium was lost from the airway; while in the kitten suctioned at 300 torr [39.9 kPa], severe damage to subepithelial and submucosal layers of the airway—with submucosal hemorrhage and separation of epithelium from underlying layers—was noted. Sackner et al[5] also noted increasing damage to tracheal and bronchial walls as suction pressure increased from 40 to 200 torr [5.3 to 20.6 kPa].

The precise suction pressure to use for removing tracheal secretions is controversial. Some authors recommend less than 100 torr [13.3 kPa],[4,6-8] while others recommend up to 200 torr [26.7 kPa].[3,5] In a response to a letter to the editor of Respiratory Care, Tom Williams[9] provided guidelines for suction setting in all age groups (Table 5), which have been supported in a number of commonly used respiratory care textbooks.[1,10-12]

Table 5. Recommended Suction-Pressure Settings[10]

Patients	Suction Range
Low-birthweight, premature infants	60-80 torr
Term infants	80-100 torr
Children	100-120 torr
Adults	120-150 torr

We believe that all of the systems evaluated in our study, including the V-VAC, meet or exceed accepted suction-pressure standards for use at the bedside. However, caution must be exercised when using these systems to perform tracheal suctioning, because each (with the exception the V-VAC) is capable of generating dangerously high suction pressures.

An argument can be made that the electric systems should incorporate a pressure gauge. The Laerdal systems do allow some regulation (the LSU system has a maximum and half-maximum suction setting); however, even the half-maximum setting exerts about 300 torr [39.9 kPa] of suctioned. The CSU system allows for regulation of suction from about 100 torr [13.3 kPa] to maximum by adjustment of the volume of air entering the system. However, with no regulator present, it is impossible to gauge with assurance what pressure is being established. The Matrx does not allow for pressure regulation, nor does it include a pressure gauge.

A large amount of variance occurred when volume of syrup suctioned in 5 seconds was evaluated; however, much less variation was noted when time required to suction 150 mL of syrup was evaluated. The variation among electric systems in the volume of syrup suctioned in 5 seconds can be attributed to the varying speeds with which maximum available suction was obtained. The Laerdal CSU achieved maximum suction rapidly and, as a result, was capable of suctioning the largest volume of syrup in 5 seconds. This variation in speed of obtaining maximum suction pressure did not significantly affect the time required to suction 150 mL of syrup; however, the Laerdal CSU again outperformed all systems compared.

The performance of the Vitalograph compared favorably with the electric systems because it was capable of maintaining a negative pressure plateau (if compressions were rapidly repeated). The same was not true for the V-VAC, in which system pressure returned to zero between each compression. Additionally, because of the type of vent used in the V-VAC for release of gas being compressed in the system, fluid began to leak from the system as the container filled. As noted, attempts to suction the 150 mL of syrup with the V-VAC were discontinued after 120 seconds.

Imitation maple syrup was used as the medium suctioned in this evaluation for two reasons: Its viscosity was high, and a consistent viscosity could be maintained. Initially, food thickener was used;

however, it was impossible to maintain a consistent viscosity over time or from batch to batch. Chunky baby food was also used, but obstruction of the 14-Fr Yankauer tube was a continual problem. The syrup we used was from a single lot to ensure consistency.

Because the V-VAC has High, Medium, and Low pressure settings, the pressure developed by the V-VAC could be controlled to a much greater extent than that of the other systems evaluated, with the exception of the Laerdal CSU. The manual movement of a compression-limiting control on the V-VAC minimized the length of the manual compression stroke, which limited pressure generation. Variations between 193 and 82 torr [25.7 and 11 kPa] were measured when the V-VAC system was empty, and slightly higher pressures were noted when it was half full.

The battery life of each of the electric systems appeared to be more than adequate for prolonged field use, provided they were recharged after use and turned off between suctioning. We continued operating these systems until the battery was completely dead, repeating the 30-second-use, 15-seconds-off sequence. The time interval before pressure dropped by 25% of maximum would appear to exceed the time of use of these systems under normal clinical conditions. In this evaluation, the Laerdal CSU system again outperformed the other systems evaluated.

As with any laboratory evaluation, the comparisons made were under ideal conditions and may not reflect actual clinical operation. The major shortcoming of this study is that only one system of each type was evaluated, and thus it is difficult to generalize these findings across all systems of a given type. In addition, we were unable to evaluate each system at suction pressure ranges consistent with those used clinically (Table 5). In spite of these shortcomings, we believe we have provided at least a gross reflection of the comparative performances of the systems evaluated.

Conclusions

Although statistically significant differences in performance were observed between the portable systems and wall suction at 300 torr [39.9 kPa], all portable systems exceeded performances required clinically. The Laerdal LSU, the Laerdal CSU, and the Matrx electric systems performed similarly to that of wall suction at 300 torr [39.9 kPa] in most comparisons. The battery life of each of these systems is adequate, provided it is appropriately recharged and turned off between uses. The Vitalograph also functioned equivalently to 300-torr [39.9-kPa] wall suction in most comparisons. The V-VAC, however, was unable to perform at the level of 300-torr [39.9-kPa] wall suction, although it proved capable of generating a maximum pressure exceeding the standard suction pressure (120-150 torr [16.0-20.0 kPa]) clinically used in adults and it could be regulated to provide appropriate suction pressure even for neonates (Table 5).

The major concern about the electric systems is the absence of regulating mechanisms capable of limiting suction pressure to clinically recommended levels. As a result, practitioners may be unaware that these systems are developing dangerously high suction pressures. Ideally, these systems should incorporate pressure gauges and limit maximum pressure to 200 torr [26.6 kPa] to prevent the adverse effects of high pressure on the pulmonary mucosa.

PRODUCT SOURCES

Portable electric suction systems:

Laerdal Medical LSU, Laerdal Medical, Armonk NY
Laerdal Medical CSU, Laerdal Medical, Armonk NY
Matrx Medical portable suction system, Matrx Medical Inc, Orchard Park NY
Vitalograph Emergency Aspirator, Vitalograph Medical Instrumentation, Lenexa KS
California Medical V-VAC, California Medical Products, Long Beach CA

Pressure transducer:

Validyne MP45-32-871 ± 880 cm H_2O, Validyne Engineering Corp, Northridge CA

Strip-chart recorder:

Hewlett-Packard System 7758-B strip-chart recorder, Hewlett-Packard, Waltham MA

Suction tube:

14-French Yankauer suction tube

REFERENCES

1. Shapiro BA, Kacmarek RM, Cane R, et al. Clinical application of respiratory care. 4th ed. Chicago: Year Book Medical Publishers Inc, 1990:181-183.

2. Frownfelter D. Chest physical therapy and airway care. In: Barnes TA, ed. Respiratory care practice. Chicago: Year Book Medical Publishers Inc, 1988:194.
3. Plum F, Dunning MF. Techniques for minimizing trauma to the tracheobronchial tree after tracheotomy. N Engl J Med 1956;254:193-200.
4. Thambiran AK, Ripley SH. Observations on tracheal trauma following suction: An experimental study. Br J Anesthesiology 1966;38:459-462.
5. Sackner MA, Lawda JF, Greeneltch N, Robinson MJ. Pathogenesis and prevention of tracheobronchial damage with suction procedures. Chest 1973;64:284-290.
6. Berman IR, Stahl WM. Prevention of hypoxia complications during endotracheal suctioning. Surgery 1968;63:586-587.
7. Fell T, Cheney FW. Prevention of hypoxia during endotracheal suction. Ann Surg 1971;174:24-28.
8. Selecky PA. Tracheostomy: A review of present day indications, complications and care. Heart Lung 1974;3:272-281.
9. Williams T. Pressures and positions in suctioning (response to a letter). Respir Care 1975;20:616-617.
10. Kacmarek RM, Mack C, Dimas S. Essentials of respiratory care. 3rd ed. Chicago: Mosby-Year Book Medical Publishers Inc, 1990:430.
11. Wilkins RL. Suctioning and airway care. In: Kacmarek RM, Stoller JK, eds. Current respiratory care. Toronto: BC Decker, 1988:91.
12. Eubanks DH, Bone RC. Comprehensive respiratory care. 2nd ed. Chicago: Mosby-Year Book Medical Publishers Inc, 1990:574.

Fracture of an Intubation Stylet: Airway Compromise and Retrieval

Erick A Kimmerling DO, James K Smith MD, and Michael F Tenholder MD

Introduction

Endotracheal intubation is not without complications,[1-3] even in a controlled setting. We report the fracture of a bare wire copper intubation stylet inside an endotracheal tube and the sequelae thereof.

Case Summary

A thin 38-year-old black man with a long-standing history of alcohol abuse, alcoholic liver disease, and associated coagulopathy was transported to the emergency room following a generalized tonic-clonic seizure. The morning of admission he complained of a stiff neck and had notable difficulty coordinating upper-body movement. A generalized seizure followed his attempt to sit upright, and he fell to the floor.

Upon arrival he was comatose. Only semi-purposeful movement was elicited in response to painful stimuli. Copious clear secretions were present in the patient's mouth. The patient was orally intubated with a size 7 endotracheal tube. With the possibility of associated trauma, a bare wire copper intubation stylet was used to facilitate insertion and avoid hyperextension of his neck. The patient was transferred to the intensive care unit on mechanical ventilation. Blood-tinged secretions were suctioned from the endotracheal tube. A portable chest radiograph showed correct endotracheal (ET) tube placement, bilateral pulmonary edema, and a fractured portion of the stylet within the distal third of the ET tube (Fig. 1).

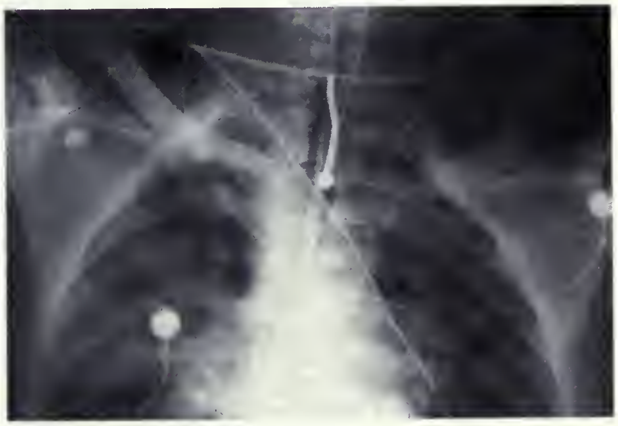


Fig. 1. A portable chest radiograph demonstrates ET tube in proper position, bilateral pulmonary edema, and the fractured piece of the stylet in the distal end of the ET tube (photograph cropped for detail).

The patient was stabilized, and retrieval of the fractured stylet was attempted using an Olympus P10 fiberoptic bronchoscope inserted via a Portex endotracheal tube adaptor. An initial unsuccessful attempt was made to retrieve it by grasping the proximal end with forceps. In a second attempt, it was successfully snared at the distal end with basket forceps (Fig. 2). The ET tube, bronchoscope, stylet fragment, and basket were then removed. The bronchoscope was immediately reinserted and an ET tube was inserted over the bronchoscope. No evidence of mucosal contusion or tracheal trauma was seen. The broken piece of the stylet measured 5.3 cm long.

Discussion

We successfully retrieved the fractured stylet with the fiberoptic bronchoscope to avoid further airway compromise. Many authors have stressed that the gold standard for foreign body removal has been the rigid bronchoscope.[4] This is the standard

---

Dr Kimmerling is a Fellow in Pulmonary Medicine, Medical College of Georgia and VA Medical Center, Augusta, Georgia. Dr Smith is Assistant Professor of Medicine, Medical College of Georgia, and Medical Director, Medical Intensive Care Unit, VA Medical Center, Augusta. Dr Tenholder is Associate Professor of Medicine, Medical College of Georgia, and Chief, Pulmonary Disease Section, VA Medical Center, Augusta. The work reported here was supported by the Research Service of the Veterans Affairs Medical Center, Augusta, Georgia.

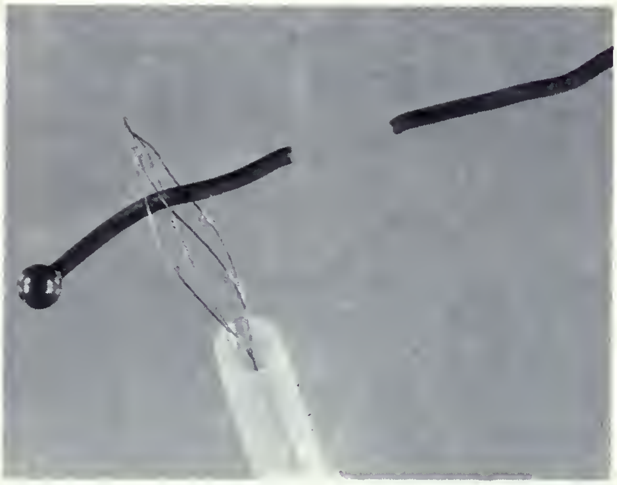


Fig. 2. The fractured 5.3-cm piece of the stylet is in the wire retrieval basket.

procedure of choice in children. We, as well as others,[5-9] have often used flexible fiberoptic bronchoscopy for foreign body retrieval in adults. This case also illustrates the benefit of fiberoptic bronchoscopy for emergency intubations. The suction channel allowed control of the bloody airway secretions. The bronchoscope was used to inspect for tracheal damage before re-insertion and allowed accurate positioning of the ET tube at an appropriate level above the carina by direct visualization.[10]

Many intubations are successfully accomplished without the use of a stylet. However, in contrast to the controlled intubation in the operating room, airway cannulation of critically ill patients should be performed with a stylet to assist in proper angulation of the endotracheal tube.[11] Many factors have been identified that will make intubation difficult and require stylet use. Upper airway anatomic or functional abnormalities occasionally present significant obstacles. Commonly recognized clinical disorders that make intubation difficult include facial and neck trauma, nasopharyngeal bleeding, goiters, foreign bodies, airway vomitus, obesity, and patients with short necks or micrognathia.[11]

Numerous techniques and specialized devices have evolved to handle the difficult intubation. Specialized adjustable stylets are available to assist in guiding endotracheal tubes into the larynx.[12] Light wands are stylets that have a light source on their end.[13,14] They transilluminate the soft tissues of the neck when placed in the trachea. These devices have been used to assist in emergency intubation in the prehospital environment and have been successful in 88% of intubation attempts.[14]

In modern intubation techniques, a stylet composed of a thin malleable alloy is placed intraluminally to aid in the insertion of the endotracheal tube. This allows shaping the ET tube and facilitates intubation in situations where the natural curve of the ET tube will not approach the vocal cords. Stylets should be used only to guide and not to fully insert the ET tube.

Traumatic injury to the delicate glottic structures is more likely if the stylet is used for forceful insertion.[1-3] The stylet should be made of a malleable alloy and should be recessed at least one-half inch inside the distal end of the ET tube.

This case illustrates a danger of reusable bare metal copper stylets. The malleable copper alloy stylet referred to in this case has different-sized spheres on either end (Fig. 3). In our experience, operators often bend the end with the larger sphere over the proximal end of the endotracheal tube to prevent the distal stylet from protruding beyond the ET tube. Fracture and aspiration of this proximal portion of the stylet (larger sphere) occurred in this case. This can happen if the stylet is inserted backwards and withdrawn from the ET tube. Either the larger sphere extended beyond the ET tube and bound on it during withdrawal, or the excessive drag of the larger sphere created sufficient linear force to fracture the stylet. This incorrect insertion caused metal failure at a site frequently flexed in the reuse of this stylet.

The possibility of fracture of the malleable copper stylet with repeated use has been considered (personal communication, Mallinckrodt Industries). Their stylet has since been changed to an aluminum alloy, which is more stress-fracture resistant. The newer stylet also measures only 34.5 cm to the curved portion, as opposed to the 37-cm length of the older stylet (Fig. 3). As an additional precaution, the improved stylet has a plastic coating over its entire length. If a fracture should occur, the coating will retain any metallic fragment. Even this added precaution has a potential risk. The present plastic-coated, malleable stylets were designed for single

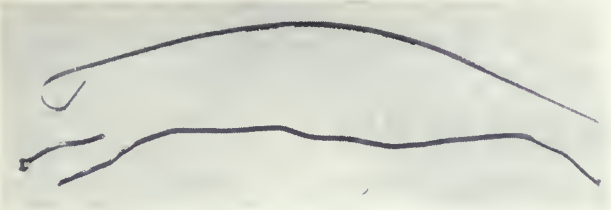


Fig. 3. The newer malleable aluminum stylet with plastic cover (top) is compared to the fractured bare metal copper stylet (bottom).

use only. It is standard practice in some hospitals to sterilize the plastic-coated stylets in a disinfectant fluid and reuse them. This practice should be reviewed and approved by the infection control policies at these medical facilities. Unfortunately, at some other institutions, these disposable stylets are being resterilized in autoclaves, which can lead to decomposition of the plastic. Shrinkage of the plastic coating allows exposure of the stylet tip, creating the potential for tip fracture or avulsion of the plastic into the airways.[15]

Many hospitals are undoubtedly continuing to reuse the bare metal copper stylets. With the potential added risk for transfer of transmittable diseases or stylet fracture, bare metal stylets should be abandoned. Sterile, plastic-coated, malleable stylets are cost-effective when viewed with respect to their overall contribution to quality care.

Stylets, although having the potential for harm, are necessary tools, especially for emergency and difficult intubations. If one understands and uses proper technique and appreciates the potential for harm, the stylet is a valuable device.

REFERENCES

1. Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy: A prospective study of 150 critically ill patients. Am J Med 1981;79:65-76.
2. Rashkin MC, Davis T. Acute complications of endotracheal intubation: Relationship to reintubation, route, urgency, and duration. Chest 1986;89:165-167.
3. Birmingham PK, Chenny FW, Ward RJ. Esophageal intubation: A review of detection techniques. Anesth Analg 1986;65:886-891.
4. Holinger PH, Holinger LD. Use of the open-tube bronchoscope in the extraction of foreign bodies. Chest 1978;73:721-724.
5. Fieselmann JF, Zavala DC, Keim LW. Removal of foreign body (two teeth) by fiberoptic bronchoscopy. Chest 1977;72:241-243.
6. McCullough PM. Wire basket removal of a large endobronchial foreign body. Chest 1985;87:270-271.
7. Lan R, Lee CH, Chiang YC, Wang WJ. Use of fiberoptic bronchoscopy to retrieve bronchial foreign bodies in adults. Am Rev Respir Dis 1989;140:1734-1737.
8. Cunanan OS. The flexible fiberoptic bronchoscope in foreign body removal. Chest 1978;73:725-726.
9. Howard TP. Foreign body extraction by means of combined rigid and flexible bronchoscopy: A case report. Respir Care 1988;33:786-789.
10. O'Brien D, Curran J, Conroy J, Bouchier-Hayes. Fibre-optic assessment of tracheal tube position: A comparison of tracheal tube position as estimated by fibre-optic bronchoscopy and by chest x-ray. Anaesthesia 1985;40:73-76.
11. Heffner JE. Managing difficult intubations in critically ill patients. Respiratory Management 1989;19:53-56.
12. Rao TLK, Mathru M, Gorski DW, et al. Experience with a new intubation guide for difficult tracheal intubation. Crit Care Med 1982;10:882-885.
13. Ellis DG, Stewart RD, Kaplan RM, et al. Success rates of blind orotracheal intubation using a transillumination technique with a lighted stylet. Ann Emerg Med 1986;15:138-142.
14. Vollmer TP, Stewart RD, Paris PM, et al. Use of a lighted stylet for guided orotracheal intubation in the prehospital setting. Ann Emerg Med 1985;14:324-328.
15. Cook WP, Schultatus RR. Obstruction of an endotracheal tube by the plastic coating sheared from a stylet. Anesthesia 1985;62:803-804.

Chest Physiotherapy in Review

Nemr Eid MD, John Buchheit MD, Michelle Neuling CRTT, and Harry Phelps CRTT

Introduction
CPT and Asthma
CPT and Pneumonia
CPT and Chronic Bronchitis
CPT and Bronchiolitis
CPT and Surgery
CPT and Atelectasis
CPT in the Neonate
CPT and Cystic Fibrosis
CPT and Bronchiectasis
Summary
References

Introduction

Chest physiotherapy (CPT) is a general term used to describe some combination of the following: postural drainage, chest-wall percussion and vibration, coughing, suctioning, and breathing exercises such as huffing, and diaphragmatic and lateral costal excursions in the spontaneously breathing patient.[1] Most authors agree that the goals of CPT are (1) to improve mucociliary clearance by preventing the accumulation of secretions or by improving their mobilization, (2) to reduce airway obstruction, and (3) to improve ventilation and gas exchange.[2]

Lack of knowledge about the indications for and the objectives of CPT can be a source of confusion, both for the physician and the respiratory caregiver. Furthermore, inappropriate orders for CPT produce time constraints on those hospital services that provide this therapy. This, in conjunction with an increasing shortage of nurses, respiratory and physical therapists compromises patient care.

Different persons have varying ideas about CPT. This is due largely to the lack of a unified definition of CPT and to the variety of procedures that are used alone or in combinations. For this reason, the literature can be confusing, and it is difficult to draw conclusions and objectively compare various studies. In this paper, we review the literature concerning the use of CPT in the presence of a number of clinical problems.

CPT and Asthma

Chest percussion and postural drainage have been used in the presence of status asthmaticus to mobilize the tenacious airway secretions frequently

---

Dr Eid is Director, Pediatric Pulmonary Medicine, and Dr Buchheit is Pediatric Chief Resident—Kosair Children's Hospital, University of Louisville, Louisville, Kentucky. When this article was prepared, Ms Neuling and Mr Phelps were respiratory therapy students at Jefferson Community College, Louisville; Ms Neuling is now at Humana Hospital Southwest, and Mr Phelps is now at Jewish Hospital—Louisville, Kentucky.

Reprints: Nemr Eid MD, Pediatric Pulmonary Medicine, Kosair Children's Hospital, 200 E Chestnut St, Louisville KY 40202.

present in this condition. This use of CPT has become controversial. Huber et al[3] (1974) studied 21 asthmatic children with mild-to-moderate airway obstruction while they underwent routine outpatient care for their asthma. The patients were allocated to two groups: 11 children were treated with clapping and vibratory compression, and 10 children were controls and did not receive this treatment. The published report of the study did not mention the length of therapy or the concomitant use of bronchodilators or other drugs. The patients who received chest percussion demonstrated a 10% increase in FEV_1 after 30 minutes of treatment ($p < 0.05$) when compared to the control patients.

Maxwell[4] (1985) reported a study of 72 asthmatic children with mucus plugging, and found CPT to be useful in resolving lung collapse. The patients received postural drainage and percussion for an average of 3.5 weeks; in many instances, the treatment was carried out by the parents after the child's discharge from the hospital. Of these 72 children, 75% showed resolution of lung collapse within 4 weeks, and most of the remaining 25% showed resolution within 12 weeks. However, no control group was available to prove that CPT was causally related to the outcome.

A review by Kiriloff et al[5] (1985) warned of CPT-induced bronchospasm in adults with asthma similar to the bronchospasm seen after CPT in chronic bronchitis patients.[6] Kiriloff et al suggested cautious use of CPT, and they found that no definitive study had been done to determine whether the desired outcome of mucus-plug mobilization can be achieved. In another review, Wissing et al[7] (1988) agreed that CPT had not been proven beneficial in asthma; they suggested its use be determined on an individual basis, with clear documentation in each case of the reason for the CPT order. Murray's 'ketchup-bottle' editorial[8] (1979) also concluded that CPT should not be used in uncomplicated asthma patients who do not produce excessive amounts of sputum, and that it should be abandoned in asthmatics who produce appreciable amounts of sputum if it is not successful in removing these secretions.

Thus, while research data on CPT and asthma are limited, it would seem prudent to avoid using CPT in asthmatics with uncomplicated acute exacerbations and to use it cautiously and selectively in patients with asthma complicated by mucus plugging. Further research is sorely needed.

CPT and Pneumonia

In the past, CPT has been used as an adjunct treatment for pneumonia. It has been assumed that if infected exudate were removed from the airway, gas exchange would be improved and the pneumonia would resolve earlier than if CPT were not used. However, there are no published studies to verify this presumption. On the contrary, evidence is increasing that CPT is detrimental to patients with pneumonia.

In a randomized trial, Graham and Bradley[9] (1978) studied 54 adults with confirmed pneumonia. For at least 3 days, half of the patients received postural drainage, percussion, and vibration for 20 minutes concomitantly with intermittent positive-pressure breathing (IPPB) and racemic epinephrine every 4 hours. No differences between the treated and untreated groups were noted in duration of fever, radiographic clearing of the pneumonia, or length of hospital stay.

Similarly, Britton et al[10] (1985) reported a study of 171 patients aged 15-75 years with acute-onset pneumonia. They were randomly assigned to study and control groups, with the study group receiving daily CPT until discharge. This consisted of postural drainage, external help with breathing, percussion, and vibration for 15-20 minutes. No other specific details regarding the CPT were described. Treatments were given by the same four physiotherapists throughout the study. Control-group patients received advice on the need for expectoration and deep breathing. The principles of pharmacotherapy management were the same for both groups. The criteria for efficacy of the CPT were duration of fever, length of hospital stay, sequential measurements of dynamic airflow, and subjective assessment of time to complete healing. No significant differences were found between the groups in duration of hospital stay, subjective assessment of healing time, or improvement of FEV_1. In fact, treated patients less than 47 years old who were smokers and patients with interstitial infiltrates, had significantly longer periods of fever and hospital stay than the nontreated controls. No explanation was given for some subsets of patients who had a longer duration of fever. The authors concluded that conventional CPT should not be applied to patients with primary pneumonia.

In a letter to the *British Medical Journal*, Stapleton[11] (1985) reported on a prospective study of 55 children hospitalized with acute lower respiratory infections. They were divided into two groups similar in age, sex, and duration of symptoms prior to admission. Apart from CPT, treatment was similar for the two groups, including the use of antibiotics and bronchodilators. The patients in the CPT group were given 5 to 15 minutes of chest percussion followed by pharyngeal suctioning two or three times daily. There were no differences between the study and control groups in duration of cough, coryza, wheeze, rhonchi, or rales. An increase in hospital stay was noted among the patients treated with CPT.

Connors et al[12] (1980) reported a study of 22 acutely ill patients with a variety of acute, nonsurgical pulmonary disorders, including 10 patients with pneumonia. CPT consisted of postural drainage and percussion by a cupped hand at a rate of 80-90 beats/minute for 10 minutes, followed by 1 to 2 minutes of vibration and chest compression. The same therapists administered all the CPT, and oxygen therapy begun prior to the study was continued throughout. Arterial blood gases (ABGs) were measured four times during the study: (1) before CPT, and after the patient had been reclining in bed with the head elevated 10 degrees for at least 10 minutes; (2) after the patient had been lying in the lateral decubitus position with the diseased lung up and the foot of the bed elevated 10 degrees for at least 10 minutes; (3) immediately after 10 minutes of chest percussion to the affected lobe; and (4) after the patient had returned to the baseline position and remained there 30 minutes. Sputum was collected throughout the study period, and the total volume was measured. The patients were divided into two groups based on their sputum volume (greater or less than 5 cc) and quality (mucoid vs mucopurulent).

The significant finding in this study was in the group who produced thin, mucoid sputum in small amounts. Those patients demonstrated a significant ($p < 0.05$) fall in mean P_{aO_2} of 16.8 torr immediately following chest percussion. No significant change in P_{aO_2} was found in 12 patients who produced moderate to large amounts of mucopurulent secretions. The authors hypothesized that the decrease in P_{aO_2} was due to ventilation-perfusion mismatch, since it did not occur in two patients who were restudied while breathing 100% oxygen. The major flaw in this study was that it included patients with a wide variety of diagnoses under the heading of ''acutely ill'' patients.

From these reports, it can be concluded that in pneumonia uncomplicated by other conditions such as bronchiectasis, CPT is not helpful and may be detrimental. According to Murray,[8] Connors et al,[12] and Sutton et al,[13] its use in this setting should be strongly discouraged.

CPT and Chronic Bronchitis

Chronic bronchitis is a condition of the adult, characterized by excessive mucus secretions in the bronchi, hypertrophy of the airways' mucus glands, recurrent bacterial infections, and intermittent airway obstruction. CPT has long been used as an adjunct treatment in removal of thick, tenacious secretions in patients with this disorder.[14] When used in spontaneously breathing patients with acute exacerbation of chronic bronchitis, CPT is found to be a safe procedure. Buscaglia and St Marie[15] (1983) reported a study of the effect of CPT on oxygen saturation in 10 patients with severe chronic obstructive pulmonary disease who were hospitalized because of acute, nonspecific exacerbation. All patients received postural drainage in the Trendelenburg position with 10 minutes of clapping and 1 to 2 minutes of vibration and chest compressions. None of the patients experienced a clinically important decrease in oxygen saturation during or after treatment. However, objective evidence on the efficacy of CPT in this disease is conflicting.

May and Munt[16] (1979) reported a comparison of the effects of a 30-minute period of chest compression and postural drainage to the results of a sham treatment (infrared lamp) in 35 patients with stable chronic bronchitis. Each patient received two methods of treatment on consecutive mornings:

(1) infrared heat administered for 10 minutes to the front and then the back of the chest, with the patient lying on his side, and (2) chest percussion for 90 seconds in each of seven drainage positions, a technique described in the *Brompton Hospital Guide to Chest Physiotherapy*.[17] Several vibrations, assisted coughing, and a brief rest period completed each sequence. While no difference was found in subjective response or in improvement of ABGs after CPT, there was a significant increase in the volume of sputum expectorated. The researchers concluded that increased sputum production is the only short-term respiratory benefit of CPT.

Bateman et al[18] (1981) further argued that CPT significantly increased clearance from peripheral lung regions in addition to increasing sputum yield. In their elegant study, six participants with stable chronic obstructive pulmonary disease (COPD) received a radioaerosol inhalation treatment and, 60 minutes later, underwent postural drainage, vibration, and cupped-hand percussion for 4 minutes out of every 5 minutes—for a total period of 20 minutes. At the end of each 4-minute sequence, the patient sat upright and was instructed to inspire deeply and then to cough for a 1-minute period. Clearance of deposited radioaerosol was then measured. Each patient completed a control study, a CPT study, and a cough study in random order separated by 1 or 2 days. During the cough study, patients were instructed to cough for 1 minute every 5 minutes. Sputum samples in each study group were collected and weighed. The initial distribution of radioaerosol was similar for all three study days. Cough alone and CPT with cough were equally effective in enhancing central lung clearance. CPT, but not cough alone, accelerated peripheral lung clearance ($p < 0.05$). The volume of sputum collected was significantly increased ($p < 0.05$) in the CPT study vs cough alone and control sputum volumes.

In a study of airway dynamics, Feldman et al[19] (1979) reported on 9 patients with cystic fibrosis and 10 patients with chronic bronchitis. Pulmonary function tests (PFTs) were performed just before CPT drainage and at 5, 15, and 45 minutes after completion of treatment. After baseline PFTs had been obtained, the patients assumed two upper-lobe drainage positions and four lower-lobe drainage positions for 5 minutes each. In each position, manual chest percussion was done for 1 minute, followed by manual vibration during four prolonged exhalations. The patients were encouraged to cough and expectorate sputum after each session. Sputum was collected during the period of postural drainage and for 45 minutes thereafter. FVC increased significantly from baseline 45 minutes after CPT in both groups ($p < 0.003$). No significant changes in FEV_1 at any time interval were seen in the chronic bronchitis group, and a significant decrease in peak expiratory flowrate (PEFR) was seen 5 minutes after CPT ($p < 0.01$), with PEFR returning to baseline after 45 minutes. Feldman et al concluded that CPT for their group of patients with chronic bronchitis resulted in a significant improvement in lung function, especially airflows measured at low lung volumes, and that the benefits of CPT were observed for as long as 45 minutes after treatment.

However, the evidence against routine use of CPT for chronic bronchitis cannot be ignored. Anthonisen and colleagues[20] (1964) reported a study of 53 inpatients with acute exacerbations of chronic bronchitis. Patients admitted to the hospital on even-numbered days of the month received daily CPT, and those admitted on odd-numbered days did not. There was no difference in pharmacologic management between the two groups. CPT was defined as expansion exercises, tapotement (tapping, percussing), and postural drainage administered daily for 10 days by a physiotherapist. No significant difference was found between the CPT and control groups in the average course of temperature, the average daily amount of expectorate, or improvement of ABGs. The authors concluded that "routine" use of CPT cannot be justified in patients with chronic bronchitis. However, they also noted that many of their patients did produce large amounts of sputum and that this may have affected their results. Furthermore, no pulmonary function values were monitored during the study.

Newton and Stephenson[21] (1978) reported studying the effects of CPT on pulmonary function in 33 patients with acute exacerbations of chronic bronchitis. For 15 minutes, patients received CPT consisting of breathing exercises, vibration, percussion in various positions, and postural drainage. This produced no change in FEV_1, FVC, specific conductance, or improvement in ABGs. A similar study by Mohsenifar et al[22] (1985) reported that 20 stable patients with chronic bronchitis showed no change in ABGs or spirometry from baseline 20 and 40 minutes after completion of either CPT (clapping, percussion, and postural drainage) for 20 minutes, or mechanical vibration for 20 minutes.

Campbell et al[6] (1975) reported a decrease in FEV_1 in 7 of 17 patients with acute exacerbation of chronic bronchitis receiving 20 minutes of percussion and vibrations. This fall in FEV_1 was corrected spontaneously within 20 minutes and could be prevented by administering salbutamol beforehand. The authors suggested that this bronchoconstriction may have been induced by physiotherapy, and they advised that CPT be used only in conjunction with the prior administration of an inhaled bronchodilator.

It would seem prudent not to routinely subject patients with chronic bronchitis to CPT, especially if they do not produce excessive amounts of secretions.[23] Murray recommended that, when there is doubt, a few trials of CPT could be carried out and then discontinued if it did not appear to be clinically efficacious.[8]

Most of the research on the use of CPT in chronic bronchitis has not taken into account an alteration in mucus viscosity induced by chronic bronchitis. The work of Puchelle et al[24] (1980) emphasized the wide range of sputum's viscoelastic properties seen in this disease. While most patients have normal or thickened mucus, other patients may have abnormally thin mucus.[24] Further research is needed to determine the significance of this variable in conjunction with CPT.

CPT and Bronchiolitis

Viral bronchiolitis is a disease characterized by inflammation of the bronchioles and seen in infants less than 2 years old. Infection of small airways results in edema and cellular infiltration throughout the bronchioles and alveolar ducts. Clinically, it is distinguished by rapid respiration, chest retractions, and wheezing. Bronchiolitis is a common cause of acute respiratory insufficiency in infants.

Although CPT is frequently used in the treatment of bronchiolitis, its efficacy has never been documented. A review of the literature revealed only two studies in the last 30 years that discussed CPT in acute bronchiolitis.[25,26] Webb et al[25] (1985) published a paper reporting their study of 90 patients with bronchiolitis who were randomly assigned into control and CPT groups. Other management decisions (eg, supplemental oxygen, and pharmacotherapy) were made independently of treatment assignment. CPT consisted of chest percussion with a cupped hand for 3 minutes in each of five postural drainage positions, followed by assisted coughing or gentle oropharyngeal suctioning performed twice daily while patients were in the hospital. A scoring method to determine the severity of illness was based on heart rate, respiratory rate, hyperinflation, use of accessory muscles of breathing, retraction, rhinitis, wheeze, cough, crepitations, and rhonchi. The investigators were unable to demonstrate any improvement in the CPT group vs the controls.

Quittell et al[26] (1988) reported studying 13 infants with culture-documented respiratory syncytial viral bronchiolitis. Pulmonary function tests (including pulmonary resistance, pulmonary compliance, and work of breathing,) were done before and after 20 minutes of CPT, with each infant serving as his own control. Although PFTs improved in some infants, they were unchanged in others, and they deteriorated in still others.

On the basis of the current literature, then, CPT seems to be of no benefit in the management of bronchiolitis, and excessive handling seems to agitate these acutely ill infants. However, more research is needed.

CPT and Surgery

Pneumonia and atelectasis are well-known postoperative respiratory complications,[27-29] and CPT is used frequently in the surgical setting to try to minimize them. A number of studies have looked objectively at this practice and have challenged its routine inclusion in postoperative orders.[30-33]

Torrington et al[30] (1984) reported a study of 53 consecutive patients undergoing Roux-en-Y gastric stapling for morbid obesity. One randomized group received chest percussion to each hemithorax for 5 to 10 minutes every 4 hours in the Trendelenburg position, whereas the other group did not. Both groups were instructed and encouraged to use incentive spirometry (IS) every 4 hours, intermittent positive-pressure breathing (IPPB) every 4 hours, a nebulized mist for 30 minutes following each IS or IPPB treatment, and deep-breathing exercises and coughing after each IS or IPPB treatment. The researchers then studied the following parameters for 48 hours: temperature, sputum production, ABG values, daily chest radiograph, FVC, and FEV_1. They found that, in patients with prior chronic lung disease, CPT actually increased the likelihood of fever, hospital cost, and patient discomfort while failing to affect the incidence of atelectasis as a postoperative complication. They were unable to demonstrate a significant difference between the two groups in sputum production, ABG values, chest radiographs, or length of hospital stay. Thus, the researchers concluded that CPT is a costly procedure both in time and money and that it offers no benefit to this subset of patients.[30]

Gormezano and Branthwaite[31] (1972) reported a significant decrease in P_{aO_2} after postural drainage and percussion in 13 postoperative patients with cardiovascular complications, but no change in 11 patients treated for respiratory failure. Similarly, Barrell and Abbas[32] (1978) showed a fall in mixed-venous PO_2 and cardiac output during CPT in patients studied several days after open heart surgery. In a study of pediatric patients undergoing cardiac surgery for congenital heart disease, Reines et al[33] (1982) reported that they had randomized 44 children, aged 3 months to 9 years, into two groups. The treatment group received postoperative pulmonary treatment that included deep breathing, suctioning of airway secretions, coughing, and CPT every 4 hours by a respiratory therapist. The CPT consisted of postural drainage with vibration and cupping in the Trendelenburg, reverse Trendelenburg, and right and left lateral decubitus positions, for a maximum of 20 minutes. The second group received only suctioning, deep breathing, and coughing. Postoperative temperatures were compared. The incidences of fever and sleeping respiratory rate were not statistically significantly different in the two groups. However, the CPT group developed atelectasis significantly more frequently ($p < 0.01$) and more severely ($p < 0.01$) than did the control group. Patients receiving CPT were also noted to have a longer hospital stay ($p = 0.05$). As possible reasons for these findings, the authors suggested that an increase in ventilation-perfusion mismatch may have been caused by the movement of mucus from peripheral lung regions, clogging central airways; and that pain may have led to splinting and decreased functional residual capacity, resulting in lung collapse.[33]

These studies suggest that CPT should not be used routinely in postoperative patients unless they have an underlying respiratory disease for which physiotherapy has been proven to be beneficial.[2,13] Paradoxically, already established postoperative atelectasis may respond to CPT,[34] which will be discussed in the next section.

CPT and Atelectasis

While CPT has long been a mainstay of therapy in patients with atelectasis, a careful study of the literature suggests that its efficacy is directly related to the etiology of the atelectasis. In asthmatics with mucus plugging and secondary atelectasis, CPT is used to aid the clearing of the plug.[4] Marini et al[34] (1979) studied 31 patients with acute lobar atelectasis. They employed CPT consisting of chest percussion and postural drainage, incentive spirometry in spontaneously breathing patients, bagged inflations in mechanically ventilated patients, coughing or suctioning, and administration of a bronchodilator. The patients were divided into two groups. The first group underwent immediate bronchoscopy after the diagnosis of atelectasis had been made, and then they received the CPT regimen every 4 hours for 48 hours. The second group received the same CPT regimen but did not undergo bronchoscopy. All patients underwent serial chest radiographs. The researchers found that the initial treatment with bronchoscopy was no more effective than CPT alone in reversing atelectasis. Of the patients who were believed to have central lung secretions with no visible air bronchogram on chest radiograph, approximately 60% of lost lung volume was restored immediately after the first CPT sessions, regardless of whether or not bronchoscopy had been performed. After 24 hours, 80% of the lost volume was restored.

Hammon and Martin[35] (1981) demonstrated the efficacy of CPT for the treatment of atelectasis in acutely ill patients. While uncontrolled, their study showed that the majority of patients who were treated with CPT improved after one treatment, as evidenced by chest radiographs taken immediately after treatments. The CPT consisted of bronchial drainage, percussion, and vibration. Finer et al[36] (1979) also showed that CPT decreased the incidence of atelectasis after extubation in neonates by improving the clearance of secretions.

However, CPT has been implicated in an increased incidence of atelectasis in pediatric and adult patients after cardiovascular surgery[34,37] or upper-abdominal surgery,[30] with up to 60% of patients developing atelectasis. This paradoxical finding is felt to occur secondary to splinting and a subsequent decrease in the functional residual capacity.

Prospective studies are needed to compare the roles of CPT and/or bronchoscopy in the management of various forms of atelectasis. In our experience, in children with either reactive airway disease or cystic fibrosis, segmental atelectasis seems to respond well to aggressive percussion, vibration, and postural drainage given for 20 minutes four times daily by either a respiratory therapist or a motivated family member. Acute lobar collapse seems less amenable to the same therapy, most likely because of mucus impaction. We find that flexible bronchoscopy is a powerful tool for dislodging impacted mucus plugs.

CPT in the Neonate

Due to their small airways, neonates are particularly sensitive to increased pulmonary secretions in association with meconium aspiration, pneumonia, bronchopulmonary dysplasia, and atelectasis.[38] In addition, many of these infants have impaired cough reflexes secondary to muscle weakness or endotracheal intubation.

CPT has been shown to be beneficial in neonates by aiding removal of secretions from the airways and preventing post-extubation atelectasis. Finer et al[36] (1979), in a prospective controlled trial, looked at 42 neonates intubated for greater than 24 hours, with routine CPT given to 21 of them at extubation, whereas the other 21 did not receive this CPT. The CPT consisted of postural drainage for the lower lobes in conjunction with percussion and vibration 1 hour prior to extubation. After extubation, an intensive course of CPT was followed: postural drainage was performed in one of the standard positions for the segments of the right upper lobes; the position was changed hourly, with vibration performed a minimum of 5 minutes out of each hour. Following chest vibration, oral suctioning was performed by a physiotherapist for the first 8 hours and subsequently by nurses trained in this technique for an additional 48 hours (every 2 hours from 8 to 24 hours postextubation, then every 3 hours for an additional 24 hours). Of the 21 infants who did not receive CPT, 8 developed atelectasis, whereas none of the 21 receiving CPT developed post-extubation atelectasis ($p < 0.01$).

Etches and Scott[39] (1978) studied six neonates with increased respiratory-tract secretions. CPT consisted of postural drainage, manual vibration, and gentle chest-wall percussion every 4 hours during the daytime. The babies underwent oropharyngeal or endotracheal suctioning every 2 hours, and secretions were collected and measured. Because the babies received CPT only with alternate suctioning, they were used as their own controls, and the amounts of secretions obtained with and without CPT were compared. Although the study population was small, the results were statistically significant ($p < 0.005$), and in all cases more secretions were removed when the babies received CPT.

Finer and Boyd[40] (1978) were able to correlate chest percussion with an improvement in oxygenation. The 20 patients with neonatal respiratory distress syndrome in their study received postural drainage with contact-heel-chest percussion for 20 minutes at a frequency of 40 per minute. Arterial blood gases were measured 15 minutes after the CPT was completed. They demonstrated an average rise in P_{aO_2} of 14.5 torr ($p < 0.001$).

However, other studies have shown that CPT can be detrimental in these infants. Holloway et al[41] (1969) reported a decrease in P_{aO_2} in 51 neonates receiving CPT. Their patients received CPT similar to that in the Finer and Boyd study, but blood samples were obtained immediately after physiotherapy was completed. After 1 hour, blood sampling was repeated, and there was no significant difference between pretreatment and posttreatment levels. Thus, the difference in sampling times may explain the different results of the two studies. Fox et al[42] (1978) also reported hypoxemia without improvement of other pulmonary functions immediately following treatment with percussion and suctioning; oxygenation returned to pretreatment levels after hyperventilation. Other reported complications of CPT in infants have been rib fracture,[43] subperiosteal hemorrhages,[44] and increased risk for severe intraventricular hemorrhage.[45]

Therefore, while CPT seems to be useful in enhancing the clearance of secretions and in preventing postextubation atelectasis, the overall clinical gain expected from this mode of treatment must be carefully assessed. The decision to use CPT must be individualized and restricted to patients who can be monitored closely.

CPT and Cystic Fibrosis

Cystic fibrosis (CF) is a genetically transmitted multisystem disease characterized by the overproduction of thick mucus due to an alteration in ionic transport across airway-surface epithelium.[46,47] It is the most common lethal genetic disease in Caucasians, with a carrier rate of 1 in 20 persons. Patients with CF tend to have excessive dehydrated mucus, which eventually leads to areas of atelectasis, hyperinflation, pneumonia, bronchiectasis, and parenchymal destruction. Failure to clear secretions results in increased airway resistance, increased work of breathing, and impaired pulmonary gas exchange.[18,48,49] Studies have revealed that the proteolytic enzymes found in these patients' mucopurulent secretions can lead to progressive destruction of the airway wall.[50] Thus, any therapy that aids in the removal of these secretions should be beneficial.

Postural drainage alone has been shown by Wong et al[51] (1977) to increase mucus clearance. They reported using radiolabeled albumin to assess mucus clearance in normal volunteers and in patients with CF. While normal volunteers demonstrated no difference in mucus clearance between upright and 25° head-down positions, CF patients had decreased clearance when upright, and clearance values approached normal when they assumed the 25° head-down position. Lorin and Denning[52] (1971) studied 17 CF patients, in whom they compared sputum volume during a regimen of postural drainage, chest percussion, vibration, and coughing with an equal period of coughing unaccompanied by CPT. They found a significant increase in the volume of sputum produced during the CPT regimen ($p < 0.0001$).

However, some authors have come to conflicting conclusions on the value of CPT in cystic fibrosis. While Denton[53] (1962) reported that percussion increased sputum production when added to postural drainage and cough, a similar study by Murphy et al[54] (1983), measuring tracheobronchial clearance with radioaerosol, showed that the addition of percussion decreased sputum clearance. De Boeck and Zinman[55] (1984) and Rossman et al[56] (1982) showed that directed, vigorous coughing exercises were as effective as postural drainage, percussion, and vibration in enhancing sputum production in CF patients.

Data on airway dynamics measurements in CF patients receiving CPT may lead to confusion. While De Boeck and Zinman[55] showed no change in sputum production, they did report an improvement in isovolume flows near V_{max25} and V_{max50} in patients receiving CPT. Tecklin and Holsclaw[57] (1975) reported a significant increase in forced vital capacity (FVC) and PEFR but no demonstrable change in FEV_1 or $FEV_{25-75\%}$. Motoyama[58] (1973) confirmed an increase in FVC and PEFR as well as an increase in V_{max25} and V_{max50} 45 minutes after postural drainage. Feldman et al[19] found significant increases in FVC, PEFR, and FEV_1. Cochrane et al[59] (1977) showed an 18% increase in specific airway conductance but only a 5% increase in FEV_1 after a 20- to 30-minute period of postural drainage and chest percussion in 23 patients who produced more than 30 mL of sputum per day.

While some differences remain when specific parameters of lung function are compared, continuation of the use of chest physical therapy in cystic fibrosis patients seems to be indicated by the literature. This is further confirmed by the studies of Desmond et al[60] (1983) and Reisman et al[61] (1988), who tested CF patients after CPT had been discontinued.

Desmond et al[60] evaluated FVC, FEV_1, and $FEF_{25-75\%}$ in 8 CF patients at the onset of their study and again after 3 weeks. During this time, the patients continued their twice-daily regimen of CPT. The second measurement was to determine the stability of the patients by comparing their PFT values to those recorded before the period had begun. The patients were then randomized into two groups; the first group stopped receiving CPT altogether for 3 more weeks, while the second group continued CPT for 3 more weeks. At the end of the second 3-week period, the patients in both groups were retested. The groups then crossed over to the opposite protocol, with the examiners blinded to which patients belonged to which group. They found a significant decrease in FVC ($p < 0.025$), FEV_1 ($p < 0.005$), and $FEF_{25-75\%}$ ($p < 0.005$) after 3 weeks without CPT. Further, it was determined that when patients renewed their CPT regimen, they returned to their previous baseline for these same pulmonary function parameters.

Reisman et al[61] performed a prospective trial to compare 30 CF patients receiving postural drainage, chest percussion, and a forced expiratory technique with 33 CF patients using the forced expiratory technique alone. The forced expiratory technique consisted of two maximal inspirations, each followed by a long, controlled, forced expiration and then three normal quiet inspirations, each followed by a long, controlled, forced expiration. The patients were followed for 3 years. Those patients who performed the forced expiratory technique alone had significant mean annual rates of decline for FEV_1 ($p < 0.001$), $FEF_{25-75\%}$ ($p < 0.001$), and Shwachman clinical score[62] ($p < 0.004$). Patients in the group receiving CPT in addition to the forced expiratory technique demonstrated a significant decline only in $FEF_{25-75\%}$ ($p < 0.03$), and their rate of decline in this parameter was not as severe as the rate in the non-CPT group. The authors concluded that pulmonary disease progressed more rapidly and pulmonary function deteriorated more in CF patients when CPT was discontinued.

Autogenic drainage, a new type of physical therapy developed in Belgium by Jean Chevalier[63] (1984), seems to be gaining popularity in many European cystic fibrosis centers. This form of CPT combines relaxed breathing techniques to collect the mucus with forceful exhalations, and cough to bring this collected mucus to the upper airway for expectoration. The principle of autogenic drainage is to balance expiratory force, intrabronchial pressure, and the stability of the bronchial walls to obtain maximal expiratory airflow without causing collapse of the airway. To be successful, autogenic drainage requires patience, practice, and a quiet atmosphere. Another device widely used in Europe is the positive expiratory pressure (PEP) mask. CPT with this mask utilizes forced expiration against a variable resistance provided by a tightly fitted mask and adjusted by valves with different-sized apertures. The PEP breathing mobilizes secretions by increasing collateral ventilation,[64] and these secretions are subsequently cleared by forced expiratory technique or coughing. Several evaluations assessing the effectiveness of PEP and autogenic drainage have been performed; they have been reviewed by Lapin[65] (1990). The PEP mask has not yet been approved by the U.S. Food and Drug Administration.

High-frequency chest compression (HFCC), a more recent form of CPT, was developed by Hansen and Warwick[66] (1990) for use in patients with CF. The equipment consists of a variable-frequency airpulse-delivery system and a nonstretchable, custom-made, inflatable vest worn by the patient. Pressure pulses are controlled by the patient and are applied during expiration. Two studies have evaluated the effectiveness of this device on mucus clearance[66] and on pulmonary function.[67] They found that HFCC appears to be better than manual CPT. Long-term, multicenter studies are needed to confirm these preliminary observations made by the device's developers.

CPT remains an important mainstay of therapy in most cystic fibrosis centers, including our own. The issue of whether CPT should be done in infants who have cystic fibrosis but no evidence of lung disease is still unresolved. Because the basic defect in CF seems to be the closure of the chloride channels at the cellular level[47] and the subsequent dehydration of mucus (which ultimately leads to bronchial obstruction and bronchiectasis), it seems logical that mobilizing these thick secretions, even before any evidence of lung disease, may help delay or prevent the onset of lung destruction. The advent of infant pulmonary function testing and the feasibility of monitoring objective parameters during or after CPT may ultimately help answer some of these questions.

CPT and Bronchiectasis

Bronchiectasis is a dilatation of peripheral bronchi in concurrence with repeated infections. Simultaneously, elastic tissue in the bronchial walls disappears, and thickening and fibrosis occur. Multiple abscesses can develop in these peribronchial areas, and these lead to excess tracheobronchial secretions and impaired mucociliary clearance.[48] Symptomatic patients have cough and copious amounts of mucopurulent sputum. Bronchiectasis characteristically follows a remitting, relapsing course. CPT is used to enhance the movement of peripheral bronchial secretions to more central airways for expectoration by coughing. However, the effectiveness of this mode of treatment has been debated.

Most data, but not all, indicate that CPT used with coughing results in more sputum production than does coughing alone.[18,68] In studies by Bateman et al (1981),[18] CPT with cough was shown to increase both central and peripheral lung clearance, whereas cough alone increased central lung clearance but was not effective in peripheral lung regions.

Specific airway dynamics have been used to study the effectiveness of CPT in bronchiectasis. In a previously mentioned study, Cochrane et al[59] (1977) demonstrated that specific airway conductance was increased significantly with only a small increase in FEV_1 in patients who produced more than 30 mL of sputum per day. Mazzocco et al[48] (1985) studied 13 patients with stable bronchiectasis to determine the effects of CPT on pulmonary function, arterial oxygenation, and sputum production—and to assess whether CPT was associated with any significant side effects. PFTs, ABGs, and sputum volumes were measured at baseline, after 10 minutes of postural drainage, after an additional 10 minutes of chest percussion and postural drainage, and 30 minutes after completion of this CPT regimen. The authors concluded CPT was beneficial in patients with bronchiectasis because it enhanced the mobilization and expectoration of sputum.

As stated by Cole (1984),[69] if CPT could break the "vicious cycle" of bronchiectasis by improving the clearance of microbial and inflammatory products—and in so doing decrease the inflammatory response of the lung—it would be most useful. However, further research must be done before that assumption can be made. For now, the weight of evidence demonstrates that in bronchiectasis, CPT is associated with enhanced clearance of secretions but not with documented improvement in pulmonary function.

Summary

It is apparent from the current literature that chest physiotherapy is indicated for and seems beneficial in cystic fibrosis and after extubation in neonates. In addition, CPT in various forms seems to offer some benefit in asthma, chronic bronchitis, bronchiectasis, and atelectasis. On the other hand, it appears to be of no benefit in pneumonia, viral bronchiolitis, and as a routine postoperative therapy. Routine requests for CPT should be discouraged; this therapy should be ordered only when there is a clear indication for it. Doctors' orders often include $beta_2$-agonist nebulization followed by CPT for a wide variety of respiratory illnesses. The perception is, If CPT doesn't help, it won't hurt. This lack of knowledge about the effectiveness of CPT in various diseases may lead to the wasting of time on inappropriate orders and, sometimes, to inadvertent medical and surgical complications, which have been extensively reviewed elsewhere.[70] Therefore, CPT should be utilized selectively when the expected benefits outweigh the inherent drawbacks of the treatment.

Furthermore, the lack of standardization of CPT in these various studies, and the different clinical and physiologic criteria to assess the benefit of CPT, may be cause for confusion. There are advantages in measuring immediate changes in selected physiologic or radiologic indices, such as PFTs, ABGs, and chest radiographs, because these are objective parameters that help to determine the response to a given treatment. The disadvantage of this type of research is the lack of a prolonged follow-up of patient outcome. Long-term studies that assess outcome or resolution of diseases are clearly superior, but they are time-consuming. In cystic fibrosis, for example, it would take years to determine whether CPT improves longevity and quality of life. Such a prospective, controlled study would be impossible to do, first because of time constraints, and second because of moral and ethical considerations, as no one is willing to withhold CPT from CF patients.

Studies such as that of Reisman et al,[61] which looked at long-term changes in PFT in CF patients after two CPT modalities, are the best that can be done currently. An ideal study to settle unresolved issues in chest physiotherapy would be a well-controlled, prospective study that takes into account immediate, short-term changes in physiologic and clinical indices, as well as long-term outcome. In addition, such a study should explain in detail the specific treatment procedures, such as type of CPT, frequency, duration, and positions. For example, in asthma, does CPT alter PFTs and ABGs immediately after a treatment, and what is the clinical outcome (degree of wheezing, length of hospital stay) in patients receiving CPT vs patients not receiving it?

The roles of humidification, aerosol beta$_2$-agonists, and other pharmacologic agents that improve airflow and mucokinesis—such as theophylline and n-acetylcysteine—in conjunction with CPT is still undetermined. Further studies should address these questions, as well as the role that CPT should play in the overall "bronchial hygiene therapy"[71] programs.

ACKNOWLEDGMENTS

The authors thank Ms Carol B Sorrels for her secretarial help and Ms Karen Kinkus for her editorial comments.

REFERENCES

1. CF MacKenzie, ed. Chest physiotherapy in the intensive care unit. Baltimore: Williams & Wilkins, 1989:31.
2. Sutton P. Chest physiotherapy: Time for reappraisal. Br J Dis Chest 1988;82:127-137.
3. Huber AL, Eggleston PA, Morgan J. Effect of chest physiotherapy on asthmatic children (abstract). J Allergy Clin Immunol 1974;53:109-110.
4. Maxwell GM. The problem of mucus plugging in children with asthma. J Asthma 1985;22:131-137.
5. Kirilloff LH, Owens GR, Rogers RM, Mazzocco MC. Does chest physical therapy work? Chest 1985;88:436-444.
6. Campbell AH, O'Connell JM, Wilson F. The effect of chest physiotherapy upon the FEV$_1$ in chronic bronchitis. Med J Austr 1975;1:33-35.
7. Wissing DR, Boggs PB, George RB. Use of respiratory care procedures in the management of hospitalized asthmatics. Ann Allergy 1988;61:407-419.
8. Murray JF. The ketchup-bottle method (editorial). N Engl J Med 1979;300:1155-1157.
9. Graham WGB, Bradley DA. Efficacy of chest physiotherapy and intermittent positive pressure breathing in the resolution of pneumonia. N Engl J Med 1978;299:624-627.
10. Britton S, Bejstedt M, Vedin L. Chest physiotherapy in primary pneumonia. Br Med J 1985;290:1703-1704.
11. Stapleton T. Chest physiotherapy in primary pneumonia (letter). Br Med J 1985;291:143.
12. Connors AF, Hammon WE, Martin RJ, Rogers RM. Chest physical therapy. The immediate effect on oxygenation in acutely-ill patients. Chest 1980;78:559-564.
13. Sutton P, Pavia D, Bateman J, Clarke S. Chest physiotherapy: A review. Eur J Respir Dis 1982;63:188-201.
14. Speir W. Outpatient management of chronic bronchitis and emphysema. Geriatrics 1976;31:77-80.
15. Buscaglia AJ, St Marie MS. Oxygen saturation during chest physiotherapy for acute exacerbation of severe chronic obstructive pulmonary disease. Respir Care 1983;28:1009-1013.
16. May DB, Munt PW. Physiologic effects of chest percussion and postural drainage in patients with stable chronic bronchitis. Chest 1979;75:29-32.
17. Gaskell DV, Webber BA. The Brompton Hospital guide to chest physiotherapy. Oxford: Blackwell Scientific Publications, 1973:9-15.
18. Bateman JRM, Newman SP, Daunt KM, Sheahan NF, Pavia D, Clarke SW. Is cough as effective as chest physiotherapy in the removal of excessive tracheobronchial secretions. Thorax 1981;36:683-687.
19. Feldman J, Traver GA, Taussig LM. Maximal expiratory flows after postural drainage. Am Rev Respir Dis 1979;119:239-245.

20. Anthonisen P, Riis P, Sigaard-Andersen T. The value of lung physiotherapy in the treatment of acute exacerbations in chronic bronchitis. Acta Med Scand 1964;175:715-719.
21. Newton DAG, Stephenson A. Effect of physiotherapy on pulmonary function. Lancet 1978;2:228-230.
22. Mohsenifar Z, Rosenberg N, Goldberg HS, Koerner SK. Mechanical vibration and conventional chest physiotherapy in outpatients with stable chronic obstructive lung disease. Chest 1985;87:483-485.
23. Hodgkin JE. The scientific status of chest physiotherapy. Respir Care 1971;26:657-659.
24. Puchelle E, Zahm JM, Sadoul P. Drugs effects on viscoelasticity of mucus. Eur J Respir Dis 1980;61(10, Suppl):195s-208s.
25. Webb M, Martin J, Cartlidge P, NG Y, Wright N. Chest physiotherapy in acute bronchiolitis. Arch Dis Child 1985;60:1078-1079.
26. Quittell LM, Wolfson MR, Schidlow DV. The effectiveness of chest physical therapy (CPT) in infants with bronchiolitis (abstract). Am Rev Respir Dis 1988;137:406.
27. Wightman JAK. A prospective survey of the incidence of post-operative pulmonary complications. Br J Surg 1968;55:85-91.
28. Laszlo G, Archer GG, Darrell JH, Dawson JM, Fletcher CM. The diagnosis and prophylaxis of pulmonary complications of surgical aspiration. Br J Surg 1973; 60:129-134.
29. Latimer RG, Dickman M, Day WC, Gum ML, Schmidt CD. Ventilation patterns and pulmonary complications after upper abdominal surgery determined by preoperative and post operative computerized spirometry and blood gas analysis. Am J Surg 1971;122:622-632.
30. Torrington K, Sorenson D, Sherwood L. Postoperative chest percussion with postural drainage in obese patients following gastric stapling. Chest 1984;86:891-895.
31. Gormezano J, Branthwaite MA. Effects of physiotherapy during intermittent positive pressure breathing: Changes in arterial blood gas tensions. Anaesthesia 1972;27:258-264.
32. Barrell SE, Abbas HM. Monitoring during physiotherapy after open heart surgery. Physiotherapy 1978;64:272-273.
33. Reines D, Sade R, Bradford B, Marshall J. Chest physiotherapy fails to prevent postoperative atelectasis in children after cardiac surgery. Ann Surg 1982;195:451-455.
34. Marini JJ, Pierson DJ, Hudson LD. Acute lobar atelectasis: A prospective comparison of fiberoptic bronchoscopy and respiratory therapy. Am Rev Respir Dis 1979;119:971-978.
35. Hammon WE, Martin RJ. Chest physical therapy for acute atelectasis. Phys Ther 1981;61:217-220.
36. Finer N, Moriartey R, Boyd J, Phillips H, Stewart A, Ulan O. Postextubation atelectasis: A retrospective review and a prospective controlled study. J Pediatr 1979;94:110-113.
37. Iverson LIG, Ecker RR, Fox HE, May IA. A comparative study of IPPB, the incentive spirometer and blow bottle: The prevention of atelectasis following cardiac surgery. Ann Thorac Surg 1978;25:197-200.
38. Mellins R. Pulmonary physiotherapy in the pediatric age group. Am Rev Respir Dis 1974;110:137-142.
39. Etches P, Scott B. Chest physiotherapy in the newborn: Effect on secretions removed. Pediatrics 1978;62:713-715.
40. Finer N, Boyd J. Chest physiotherapy in the neonate: A controlled study. Pediatrics 1978;61:282-285.
41. Holloway R, Adams E, Desai S, Thambiran A. Effect of chest physiotherapy on blood gases of neonates treated by intermittent positive pressure respiration. Thorax 1969;24:421-426.
42. Fox WW, Schwartz J, Shaffer T. Pulmonary physiotherapy in neonates: Physiologic changes and respiratory management. J Pediatr 1978;92:977-981.
43. Purohit DM, Caldwell C, Levkoff AH. Multiple rib fractures due to physiotherapy in a neonate with hyaline membrane disease. Am J Dis Child 1975;129:1103-1104.
44. Wood B. Infant ribs: Generalized periosteal reaction resulting from vibrator chest physiotherapy. Radiology 1987;162:811-812.
45. Ravel D, Cuevas D, Mora A, Yeh TF, Pildes RS. The efficacy of chest physiotherapy (CPT) on the first postnatal day in infants with RDS (abstract). Pediatr Res 1985;19(Suppl):359A.
46. Boucher RC, Stutts MJ, Knowles MR, et al. Na^+ transport in cystic fibrosis respiratory epithelia: Abnormal basal rate and response to adenylate cyclase activator. J Clin Invest 1986;78:1245-1252.
47. Frizzell RA, Rechkemmer G, Shoemaker RL. Altered regulation of airway epithelial cell chloride channels in cystic fibrosis. Science 1986;233:558-560.
48. Mazzocco M, Kirilloff L, Owens G, Rogers R. Chest percussion and postural drainage in patients with bronchiectasis. Chest 1985;88:360-363.
49. Zach M, Oberwaldner B. Chest physiotherapy—The mechanical approach to anti-infective therapy in cystic fibrosis. Infection 1987;5:381-384.
50. Bruce MC, Poncz L, Klinger JD, Stern RC, Tomashefski JF, Dearborn DG. Biochemical and pathologic evidence for proteolytic destruction of lung connective tissue in cystic fibrosis. Am Rev Respir Dis 1985;132:529-536.
51. Wong J, Keens T, Wannamaker E, Crozier D, Levinson H, Aspin N. Effects of gravity in tracheal transport rates in normal subjects and in patients with cystic fibrosis. Pediatrics 1977;60:146-152.
52. Lorin ML, Denning CR. Evaluation of postural drainage by measurement of sputum volume and consistency. Am J Phys Med 1971;50:215-219.
53. Denton R. Bronchial secretions in cystic fibrosis. Am Rev Respir Dis 1962;86:41-46.

54. Murphy MB, Concannon D, FitzGerald M. Chest percussion: Help or hinderance to postural drainage. Ir Med J 1983;76:189-190.
55. De Boeck C, Zinman R. Cough versus chest physiotherapy. Am Rev Respir Dis 1984;129:182-184.
56. Rossman CM, Waldes R, Sampson D, Newhouse M. Effect of chest physiotherapy on the removal of mucus in patients with cystic fibrosis. Am Rev Respir Dis 1982;126:131-135.
57. Tecklin J, Holsclaw D. Evaluation of bronchial drainage in patients with CF. Phys Ther 1975;55:1081-1084.
58. Motoyama EK. Assessment of lower airway obstruction in cystic fibrosis. In: JA Mongos, RC Talamo, eds. Fundamental problems of CF and related diseases. New York: Intercontinental Medical Book Corp, 1973:335.
59. Cochrane GM, Webber BA, Clarke SW. Effects of sputum on pulmonary function. Br Med J 1977;2:1180-1183.
60. Desmond K, Schwenk F, Thomas E, Beaudry P, Coates A. Immediate and long-term effects of chest physiotherapy in patients with cystic fibrosis. J Pediatr 1983;103:538-542.
61. Reisman J, Rivington-Law B, Corey M, et al. Role of conventional therapy in cystic fibrsis. J Pediatr 1988; 113:632-636.
62. Shwachman H. Therapy of cystic fibrosis of the pancreas. Pediatrics 1960;25:155-163.
63. Chevalier J. Autogenic drainage. In: Lawson D, ed. Cystic fibrosis: Horizons. Chichester: John Wiley, 1984:235.
64. Andersen JB, Qvist J, Kann T. Recruiting collapsed lung through collateral channels with positive end expiratory pressure. Scand J Respir Dis 1979;60:260-266.
65. Lapin A. Chest physical therapy in cystic fibrosis: A review. Cardiopul Phys Ther 1990;1:11-13.
66. Hansen LG, Warwick WJ. High-frequency chest percussion system to aid clearance of mucus from the lung. Biomed Instrum Technol 1990;24:289-294.
67. Warwick W, Hansen L. Vest bronchial drainage therapy 2 year follow-up (abstract). Pediatr Pulmonol 1990; 5(Suppl):251.
68. Darrow G, Anthonisen N. Physiotherapy in hospitalized medical patients. Am Rev Respir Dis 1980;122:155-158.
69. Cole PJ, ed. Strategies for the management of chronic bronchial sepsis. Oxford: Medicine Publishing Foundation, 1984.
70. Tyler ML. Complications of positioning and chest physiotherapy. Respir Care 1982;27:458-466.
71. Shapiro BA, Harrison RA, Trout CA. Clinical application of respiratory care. 2nd ed. Chicago: Year Book Medical Publishers, 1979:155-232.

Donald F Egan Scientific Lecture

Twenty-Five Years of Progress in Hyaline Membrane Disease

Mary Ellen Avery MD

Introduction

I want to tell you some of the story of the evolution of our understanding of pulmonary surfactants and their role in stabilizing the peripheral air spaces of the lung. As you doubtless know, they are, in fact, antiatelectasis factors. I will then turn to surfactant replacement therapy, the major clinical advance that has led to a significant reduction of deaths of live-born premature infants from respiratory distress syndrome, or hyaline membrane disease. Approximately 30,000 infants have been treated in 500 hospitals in 33 countries.

History

Insight into surface forces in lungs began with the observations of von Neergard, the Swiss physician who in 1929 wrote a paper entitled, "New Notions on a Fundamental Principle of Respiratory Mechanics: The Retractile Force of the Lung, Dependent on the Surface Tension of the Alveoli." He speculated that the atelectasis of the newborn might be due to "considerable retractive force of surface tension in the lungs." He carried out experiments demonstrating that an excised lung inflated with air had a considerably greater transpulmonary pressure than the same lung expanded to the same volume with liquid. That simple, straightforward experiment was reproduced independently in the 1950s by Mead and others at the Harvard School of Public Health. The stage was set for understanding the unique properties of the alveolar lining layer: When expanded to augment the elastic recoil of the lung and when compressed to reduce surface tension so that alveoli arranged in parallel can remain stable and thus not go to an airless state.

One way to demonstrate the effect of this phenomenon is to inflate a moderately premature lamb's lung and notice that it inflates very uniformly, but on deflation only the more cephalad portions remain aerated while the more caudad portions go to airlessness. If we remember the cephalocaudal course of embryonic development, it is apparent that here even in the lung one sees a more mature cephalad portion and a less mature caudad portion that in the absence of surfactant goes to airlessness.

Pathologists in the late 1940s, studying lungs at autopsy, noted that the appearance of lungs of premature infants who died with respiratory distress appeared liver-like and when expanded with air showed a "swiss-cheese-pattern" of overdistended air spaces and atelectasis. Gruenwald, one of those pathologists, inflated the lungs with liquid and found that with liquid inflation the air spaces were more evenly distended. Indeed, he speculated that abnormal surface forces could be operating to produce this difference.

Meanwhile, clinicians were becoming more and more interested in the behavior of these premature babies after birth and noted that they had marked retractions and rapid respiratory rates. The infants often breathed reasonably normally for the first few hours, but then a progressive respiratory distress could lead to death within the first hours of life,

---

Dr Avery is Thomas Morgan Rotch Professor of Pediatrics, Harvard Medical School, Boston, Massachusetts.

This paper is based on a transcript of The Donald F Egan Scientific Lecture delivered by Dr Avery at the Annual Meeting of the American Association for Respiratory Care in New Orleans, Louisiana on December 9, 1990.

Reprints: Mary Ellen Avery MD, 221 Longwood Ave, Boston MA 02115.

but more commonly between the second and third day. If infants survived that third day, they often recovered completely. The membranes associated with the name hyaline membrane disease were not there at birth, but were acquired from reaction to injury of distension of air spaces in the first hours of life. Thus, the liquid-filled lungs of the fetus appeared normal, but after air breathing the lungs developed an uneven distribution of air, and after a few hours edema and membrane formation appeared in the ventilated air spaces.

Now we turn to a totally different environment, the chemical defense establishment in Porton, England, where Pattle was assigned to study the role of antifoam agents in the prevention of the pulmonary edema that could be induced by certain war gases. He devised a technique by which he could measure the stability of bubbles expressed from the lung as they were suspended in a drop of saline. He could examine the life span of this drop, so to speak, through a microscope. He noted that bubbles expressed from the lung seemed to have a much longer life span than bubbles expressed from serum or other tissues. He wrote a description of these findings in the now famous paper called, ''Properties, Function and Origin of the Alveolar Lining Layer,'' which was published in 1958.

A turning point in all this work arose from the Army chemical center in Edgewood where Clements was also interested in antifoam agents. He devised a method to measure surface tension in a somewhat more sophisticated way with a Wilhelmy balance that allowed him to ascertain the changes in surface tension with changes in surface area. I had known of Pattle's work from a preliminary publication of his in *Nature* in 1955, and at Christmas 1956 I heard of Clements' work. I also had known Gruenwald and of his interest in the possibility of abnormal surface forces in lungs of infants who died of hyaline membrane disease. It seemed only natural then to learn how to measure surface tension of material expressed from the lungs. The generosity of John Clements in telling me how to proceed, made it possible for me to examine the behavior of materials from lungs of infants who had died.

I was at that time a Fellow in Neonatology at the Boston Lying-In Hospital, and had access to autopsy material. I had noted that there was never any foam in the airways of infants who died of hyaline membrane disease, while foam was usually abundant in other autopsy specimens. In fact, that was the major observation. However, one does not publish a manuscript that says simply ''some infant lungs do not have foam.'' It was necessary to learn how to measure the behavior of these lungs with pressure-volume curves and also to ascertain the presence or absence of surface-tension reducing substances. We found that measurements of surface tension of lung extracts confirmed the presence of a very surface-active substance in lungs of most infants over 1.2 kg and in children and adults. In lung extracts of immature infants and those dying of hyaline membrane disease at any age, the ability to achieve low surface tension was not demonstrable. We wrote that this deficiency of surface-active material may be significant in the pathogenesis of hyaline membrane disease. That paper was published in 1959.

It is the events of the next 25-30 years that I intend to focus on because we have moved from those very simple observations to an understanding of the chemical and physical properties of the alveolar lining layer, and even now have totally synthetic materials that can be instilled into infants' lungs to carry them over the critical first few days until they synthesize pulmonary surfactants.

A landmark publication in 1973 by Gluck and colleagues demonstrated that in the last trimester of pregnancy the maturity of the fetal lung can be assessed by measuring components of the surfactant in the amniotic fluid. You doubtless have heard of the lecithin-sphingomyelin (L-S) ratio, which takes advantage of the fact that the lecithins increase disproportionately to sphingomyelin at the time the lungs achieve alveolar stability. This assay allows prenatal diagnosis of infants at risk of having surfactant deficiencies after birth. Subsequently, it was demonstrated that it is possible to accelerate synthesis of the surfactants with prenatally administered glucocorticoids; the subsequent hormonal regulation of surfactant synthesis and secretion has been extensively explored.

Surfactant Replacement

During the 1960s and 1970s, a number of investigators were interested in finding ways to replace the missing components of surfactant, first by aerosol in 1964, with only limited success, and later and dramatically by direct instillation of the materials into the lung by Fujiwara and associates in Japan. Their work had followed a decade of careful study of various mixtures of components of the surfactant, tested in vivo and in vitro, and finally with the invention of a recipe that was very effective in the animal model and also in a small series of humans, the results of which were published in *Lancet* in 1980. They realized that no mixture that was only phospholipids would have the requisite surface properties to stabilize airways effectively. Lung-associated proteins are required for the appropriate adsorption to the surface and changes in surface tension with area. The Fujiwara recipe was first called TA surfactant (after Tokyo, where the pharmaceutical house was located, and Akita, where Fujiwara was working at the time). What distinguished Fujiwara's experience from that of the others was that he used natural surfactants, that is, material expressed from cow's lung, and that he modified and instilled them as a liquid into the trachea. After the instillation of 3-5 mL of material, he could demonstrate distribution in all lobes of the lung, and, impressively, a prompt increase in oxygenation.

I find it of some interest that these dramatic observations were not immediately acclaimed, probably in part because the published experience was not in the format of a prospective, randomized, controlled clinical trial. Nevertheless, Fujiwara's publication stimulated many investigators in various parts of the world to conduct those randomized controlled trials, and at the latest count there had been 33 such trials published, including an extensive one by Fujiwara himself in the November 1990 issue of *Pediatrics*.

Meanwhile, others have pursued the possibility of using surfactants from other sources, such as human amniotic fluid. Merritt and Hallman in San Diego showed impressive results in lessening the severity of respiratory distress syndrome and also bronchopulmonary dysplasia, the chronic lung disease that follows injury in the first days of life. A porcine material was studied by Robertson and colleagues in Europe, and others have used calf lung lavage as the primary source of material. One totally synthetic mixture, Exosurf, was licensed in the United States in mid-1989. Exosurf was invented by Clements, who proposed that the major phospholipid in pulmonary surfactant, dipalmitoyl phosphatidyl choline, could be made to adsorb to the surface with the administration of small amounts of detergent. Controlled clinical trials for this material were initiated in October 1987 but have not been published to date,* despite the fact that the material is now licensed. The materials in Exosurf do not, in fact, stabilize the air spaces by themselves; but because they contain the major phospholipid in natural surfactant, they probably induce synthesis by enhancing substrate availability.

On the other hand, the natural surfactants, which have the surfactant-associated proteins in them, improve gas exchange more promptly than the phospholipids alone. Importantly, however, the surfactant protein SP-A, which is the last to appear in gestation and is missing in infants with hyaline membrane disease, is not present in any of the replacement mixtures that have been studied so far. The explanation for the efficacy of the SP-A-deficient replacement mixtures is that one function of SP-A is to facilitate the movement of the material from its site of synthesis in the alveolar Type II cell to the surface. Exogenous surfactants do not need to be brought to the surface from the cells.

Clinical Experience

As I mentioned earlier, it has been estimated that approximately 30,000 infants in 500 hospitals in Europe, Japan, and North America have been treated with one or another of the available surfactants. The issues surrounding treatment concern the most appropriate time for administration, as soon as possible after birth or within 2 hours after birth; it does not seem to make much difference. Some benefit is found when given later, although most trials favor administration within a few hours of birth. The trials have involved an evaluation of a single dose or up to 4 doses. A number of infants do not respond; and others actually have an initial response but then relapse. Such observations suggest that some babies need more doses, and now the administration of up to 4 doses over the first 48 hours of life is widely practiced.

---

*The results of these trials have since been reported. See Corbet et al in Suggested Readings.

There are other important issues with respect to the manner in which the surfactants are instilled through an endotracheal tube. They are much more efficiently distributed that way than they are by aerosol, and it is remarkable that very small amounts, 3-5 mL, can spread so effectively throughout these lungs. Of course, one of the properties of surfactant is that it does spread on surfaces whose surface tension is relatively higher, such as in the lungs of infants with respiratory distress syndrome. Some infants have an immediate adverse response to surfactant, and colleagues in Sweden have even shown cessation of electrical activity of the brain when the materials are pushed as a bolus into the trachea. This is not surprising because the material can effectively obstruct the upper airway. Thus, we administer the materials very slowly, even over a period as long as half an hour, with a neonatologist at the bedside during that entire time. One of the important reasons to have the materials administered so carefully, is that when they do reach the terminal air spaces the oxygen requirement falls immediately as does the pressure requirement. Thus, one has to keep one's hand on the knobs of the ventilator to make the adjustments appropriately. The dangers of hyperoxia in premature infants are well known to everyone, and the dangers of high pressure are presumably of paramount importance in the lung injury that can lead to bronchopulmonary dysplasia. Thus, it is not appropriate to administer surfactants and walk out to lunch. It is absolutely critical that these materials be administered with full knowledge of what their immediate and even delayed effects can be on the lung.

A significant reduction in deaths, in severity of hyaline membrane disease, and in chronic lung disease, has resulted from the appropriate administration of surfactant particularly in the recent studies that have involved more than a single dose.

Future Uses of Surfactant

There are some exciting ideas for future uses of these materials. It is obvious that they can be used as a vehicle to deliver drugs to the peripheral air spaces. If we know drugs are not toxic when administered by aerosol, we can surmise that they will be nontoxic when delivered with pulmonary surfactants as the vehicle and can reach the infecting organisms in higher concentration than they can by aerosol. Thus, the surfactants are possibly a useful vehicle for the delivery of drugs such as pentamidine for the treatment of *Pneumocystis carinii* pneumonia. It is also evident that the materials, by virtue of their spreading, are in a sense mucolytic. There have been anecdotal reports of responses in some patients with severe asthma and in some instances of pneumonia. These experiences to the best of my knowledge have not been systematically controlled but are of interest, and surely we will hear more about surfactants, not only for premature infants with immature lungs, but for children and adults under some circumstances.

Conclusion

Finally, I would like to report to you that in the United States deaths of infants with hyaline membrane disease were reduced approximately 50% during the period from the late 1970s to the late 1980s by better use of ventilators and by the ability to accelerate lung maturation with prenatal glucocorticoids (such as dexamethasone) given to mothers 48 hours before delivery. Since then there has been a further reduction in mortality, particularly for the very-low-birthweight infants, that even now has made hyaline membrane disease no longer the leading cause of death of liveborn premature infants. Malformations have achieved that number one position. However, surfactant replacement is not a substitute for all other aspects of supportive care for low-birthweight infants.

We cannot end a presentation such as this without saying that the major goal has to be the prevention of preterm birth. Because it is inevitable that some babies will be born prematurely, it is satisfying to know that we have some effective therapies. It is also of interest that this is the first time a totally new kind of drug has been prepared specifically for low-birthweight infants and administered by a novel route—direct instillation to the trachea. Surfactant replacement is here to stay.

SUGGESTED READINGS

Avery ME, Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. Am J Dis Child 1959;97:517-523.

Charon A, Taeusch HW, Fitzgibbon C, et al. Factors associated with surfactant treatment response in infants with severe respiratory distress syndrome. Pediatrics 1989;83:348.

Clements JA. Surface tension of lung extracts. Am J Physiol 1956;187:592.

Comroe JH Jr. Retrospectroscope: Insights into medical discovery. Menlo Park CA: von Gehr Press, 1977:140-161.

Corbet A, Bucciarelli R, Goldman S, et al. Decreased mortality rate among small premature infants treated at birth with a single dose of surfactant: A multicenter controlled trial. J Pediar 1991; 118:277-284.

Enhorning G, Shennan A, Possmayer F, et al. Prevention of neonatal respiratory distress syndrome by tracheal instillation of surfactant: A randomized clinical trial. Pediatrics 1985;76:145-153.

Farrell PM, Avery ME. Hyaline membrane disease: State of the art. Am Rev Respir Dis 1975;111:657-688.

Floros J. Sixty years of surfactant research (meeting report). Am J Physiol 1990;2:238-240.

Fujiwara T, Maeta H, Chida S, et al. Artificial surfactant therapy in hyaline membrane disease. Lancet 1980;1:55-59.

Fujiwara T, Konishi M, Chida S, et al. Surfactant replacement therapy with a single postventilatory dose of a reconstituted bovine surfactant in preterm neonates with respiratory distress syndrome: Final analysis of a multicenter, double-blind, randomized trial and comparison with similar trials. Pediatrics 1990;86:753.

Gluck L, Kulovich MV. Lecithin/sphingomyelin ratios in amniotic fluid in normal and abnormal pregnancies. Am J Obstet Gynecol 1973;115:539.

Hallman M, Merritt A, Jarvenpaa A-L, et al. Exogenous human surfactant for treatment of severe respiratory distress syndrome: A randomized prospective clinical trial. J Pediatr 1985;106:963-969.

Hennes HM, Lee MB Rimm AA, Shapiro DL. Surfactant replacement therapy in respiratory distress syndrome: Meta-analysis of clinical trials of single dose surfactant extracts. Am J Dis Child 1991;145:102.

Jobe A, Ikegami M, Jacobs H, et al. Permeability of premature lamb lungs to protein and the effect of surfactant on that permeability. J Appl Physiol 1983;55:169-176.

Mead J, Whittenberger JL, Radford EP Jr. Surface tension as a factor in pulmonary volume-pressure hysteresis. J Appl Physiol 1957;10:191.

Pattle RE. Properties, function and origin of the alveolar lining layer. Nature 1955;175:1125.

Pattle RE. Properties, function and origin of the alveolar lining layer. Proc Royal Soc, London 1958;148:217.

Shapiro DL, Notter RH, Morin FC III, et al. Double-blind randomized trial of a calf lung surfactant extract administered at birth to very premature infants for prevention of respiratory distress syndrome. Pediatrics 1985;76:593-599.

Shapiro DL, Notter RH. Surfactant replacement theory. New York: ALAN R LISS INC,1989.

Suzuki Y, Curstedt T, Grossmann G, et al. The role of the low-molecular weight ($\leqslant$15000 daltons) apoproteins of pulmonary surfactant. Eur J Respir Dis 1986;69:336-345.

Long-Term Mechanical Ventilation as Elective Therapy

Roger S Goldstein MD and David J Pierson MD

This month's issue of the Journal features two articles from the second half of the 1990 AARC symposium on long-term mechanical ventilation (LTMV).[1] They are grouped to reflect the important emerging dimension of elective mechanical ventilatory support—for patients in whom it might be predicted that without such interventions their clinical course would be one of progressive deterioration, resulting at best in emergency ventilation and management in the intensive care unit (ICU), but at worst in premature death in the absence of prompt mechanical support.

These papers emphasize information that is highly relevant to both respiratory care practitioners and physicians. Stoller[2] first reviews the background that has emerged during the last 10 years to suggest that the respiratory muscles have in common with other skeletal muscles the tendency to fatigue, and that this fatigue by definition can be relieved by unloading or resting the muscles. Although there is some evidence that a situation akin to fatigue may be observed during weaning trials, whether a state of so-called chronic fatigue in fact exists remains unproven. This notion remains attractive, however, to those who approach the management of such patients with inspiratory muscle rest.

Stoller's paper ends with a review of some articles describing application of negative-pressure ventilation to patients with severe chronic obstructive pulmonary disease (COPD). Although there is evidence that COPD patients who are 'unloaded' with either negative- or positive-pressure ventilation demonstrate reduced inspiratory muscle activity during wakefulness as assessed by electromyogram(EMG), to date there has been no prospective, controlled trial of LTMV that has demonstrated any improvement whatsoever in clinical function in this patient population. Whether this relates to the technology currently available or to flaws in the rationale for its application remains to be seen.

Use of mechanical ventilation equipment in the home setting clearly places different demands on equipment from the demands encountered in the ICU. Such equipment must be simple to operate, designed to be physically suitable for the home environment, and relatively inexpensive. Important progress is being made in the development of such equipment, and, undoubtedly, the next few years will bring a greater choice in ventilatory equipment appropriate for home use.

Increasing attention has been focused on the interface between machine and patient. This attention has resulted in the development of newer types of cuirass and face mask, for negative- and positive-pressure ventilation, respectively. Interesting prototypes are being evaluated and will likely be given greater prominence if a third symposium is held 5 years hence. The potential for nonconventional approaches to mechanical support, such as proportional-assist ventilation and external high-frequency oscillation, will likely be reported on in this journal over the next few years. The second paper, by Goldstein and Avendano,[3] provides a

---

Dr Pierson is Professor of Medicine, University of Washington, and Medical Director, Respiratory Care Department, Harborview Medical Center—Seattle, Washington. Dr Goldstein is Associate Professor of Medicine, University of Toronto, and Director, Respiratory Medicine, West Park Hospital—Toronto, Ontario, Canada.

clinical perspective on existing applications of home LTMV. In contrast to patients with COPD, in whom the underlying pulmonary parenchymal disease often continues to progressively worsen despite mechanical ventilation, those with thoracic restrictive diseases such as kyphoscoliosis or neuromuscular disease may expect a very good response to elective nocturnal noninvasive support by either negative or positive pressure. Such patients not only reduce their inspiratory muscle EMG when on the ventilator but also stabilize gas exchange during sleep, improve their daytime arterial blood gases, and achieve better daytime function. Such persons often return to full-time employment, education, or home activities, and spend fewer days in hospital, with almost no days in the ICU, in the first year following initiation of ventilator support as compared to the year prior to initiation of elective LTMV.

In all, the future of LTMV at home seems bright. Although clear criteria for patient selection and the timing for elective ventilation remain to be established, it has been useful to revisit LTMV 5 years after the original symposium. The Journal's readers can look forward to an equally worthwhile symposium and series of articles 5 years from now.

REFERENCES

1. Pierson DJ, Goldstein RS. Long-term mechanical ventilation revisited. Respir Care 1991;36:184-185.
2. Stoller JK. Physiologic rationale for resting the ventilatory muscles. Respir Care 1991;36:290-296.
3. Goldstein RS, Avendano MA. Long-term mechanical ventilation as elective therapy: Clinical status and future prospects. Respir Care 1991;36:297-304.

Physiologic Rationale for Resting the Ventilatory Muscles

James K Stoller MD

Introduction

Because ventilatory muscle fatigue has come to be viewed as the mechanism mediating ventilator dependency, ventilatory muscle rest has gained increasing popularity as a strategy for enhancing weaning and functional status in patients with hypercapnia. To date, ventilatory muscle rest has been undertaken in a wide spectrum of patients whose ventilatory muscle insufficiency is based on:

1. decreased ventilatory muscle strength and/or endurance (eg, neuromuscular diseases such as myasthenia gravis, muscular dystrophy, Guillain-Barré syndrome, post-poliomyelitis respiratory insufficiency, and acid maltase deficiency),
2. chronic obstructive pulmonary disease (COPD), and
3. increased demands on ventilatory muscle output that outstrip the capabilities of the muscles (eg, COPD, kyphoscoliosis, and obesity).

This paper reviews the physiologic rationale for resting the ventilatory muscles, considering first the physiology of respiratory muscles and then defining and describing the clinical spectrum of respiratory muscle fatigue. The third section reviews evidence that inspiratory muscle fatigue portends hypercapnia and failure to wean. As a final line of evidence justifying ventilatory muscle rest, the paper reviews evidence that mechanical ventilation can lessen inspiratory muscle activity and improve inspiratory muscle function and ventilation.

The Physiology of Respiratory Muscles

Working in concert with muscles of the rib cage (including the external intercostals, the interchondral portion of the internal intercostals, and the scalene muscles), the diaphragm is the major inspiratory muscle. Like skeletal muscle in general, the diaphragm is composed of a mixture of muscle fiber types, in a distribution especially suited to the diaphragm's unique endurance demands.[1-3] Table 1 summarizes muscle fiber types and their key characteristics, emphasizing that Type-1 fibers are slow-twitch, are recruited first, and generate the least force but are the most resistant to fatigue. Type 2b and 2a fibers are less fatigue-resistant but serve fast-twitch muscular activity. To the extent that the major function of the diaphragm is to provide inspiratory endurance, it is appropriate that Type-1 fibers comprise approximately 55 ± 5% of the muscle fibers of the human diaphragm. Type 2a and 2b fibers comprise the remaining muscle fibers (20 ± 6% and 25 ± 3%, respectively). Although the composition of intercostal muscles has been less well studied, available information suggests that the fiber-type composition is similar to that of the diaphragm.[1]

Respiratory Muscle Fatigue

The definition of respiratory muscle fatigue has evolved in concert with increasing evidence that ventilatory muscle fatigue mediates hypercapnia and ventilatory failure. Specifically, earlier definitions of muscle fatigue emphasized the inability to generate force:[4]

Dr Stoller is Head, Section of Respiratory Therapy, and Staff Physician, Department of Pulmonary Disease, The Cleveland Clinic Foundation, Cleveland, Ohio.

A version of this paper was presented by Dr Stoller during the Long-Term Mechanical Ventilation Symposium at the 1990 Annual Meeting of the American Association for Respiratory Care in New Orleans, Louisiana.

Reprints: James K Stoller MD, Department of Pulmonary Disease, A90, One Clinic Center, The Cleveland Clinic Foundation, Cleveland OH 44195.

Table 1. Summary of Muscle-Fiber Types and Their Characteristics

Fiber Type	Twitch Type	Oxidative Enzyme	Glycogen	Recruitment	Fatigue Resistant	Force
Type I	Slow	High	Low	First	Highest	Lowest
Type 2b	Fast	Low	High	Last	Lowest	Highest
Type 2a	Fast	High	High	Intermediate	Intermediate	Intermediate

> Muscle fatigue is a condition in which a muscle is unable to continue to develop or maintain a predetermined force.

A more recent definition, framed by the Respiratory Muscle Fatigue Workshop Group, emphasizes a loss of capacity to generate force and the restorative benefits of rest:[1]

> Muscle fatigue is a condition in which there is a *loss in the capacity for developing force* and/or velocity of a muscle, resulting from muscle activity under load and which is *reversible by rest.* (Italics added.)

In considering the determinants of ventilatory muscle fatigue, assessing the balance between demand factors and supply factors is useful. As presented in Table 2, demand factors include increased work of breathing (WOB), increased strength of muscular contraction, and decreased efficiency, while features associated with supplying the ventilatory muscles with necessary substrates include the oxygen content of blood, the inspiratory muscle blood flow, the general nutritional status, and the muscles' ability to extract energy from supplied substrates. In the context of this "balance of power," diseases that manifest ventilatory muscle fatigue can be categorized as those in which there is decreased muscle strength and/or endurance vs those in which muscular demands are increased and may outstrip strength and endurance capabilities. Examples of the former include neuromuscular diseases (such as myasthenia gravis, muscular dystrophies, amyotrophic lateral sclerosis, post-poliomyelitis respiratory insufficiency, and acid maltase deficiency) and shock states in which muscle diaphragm perfusion is diminished. Diseases in which ventilatory muscle demands are increased and may outstrip supply include COPD (in which hyperinflation may place the inspiratory muscles at a mechanical disadvantage, with concomitantly decreased efficiency and increased oxygen cost of breathing [O_2COB]),[4] kyphoscoliosis,[5] and obesity.[6] By virtue of hyperinflation that compromises the diaphragm's function as a power generator, hypercapnic COPD reflects contributions of both decreased muscle strength and endurance and increased muscle demands. As discussed in an accompanying paper in this symposium,[7] the lung component of resting WOB is increased in emphysema,[8,9] obesity,[6] and kyphoscoliosis.[5] Similarly, as a measure of demands on the respiratory muscles, the O_2COB is increased in asthma[10] and emphysema.[11] That oxygen demands for ventilatory muscle function can outstrip supply has been suggested by Macklem[4] and is depicted in Figure 1; the O_2COB rises steeply with increasing

Table 2. Determinants of Ventilatory Muscle Failure: The Balance of Power*

Demand Factors	Supply Factor
Work of breathing	Oxygen content of blood
Strength of muscle contraction	Inspiratory muscle blood flow
Efficiency	Nutrition
	Ability to extract energy

*Adapted from Reference 4, with permission.

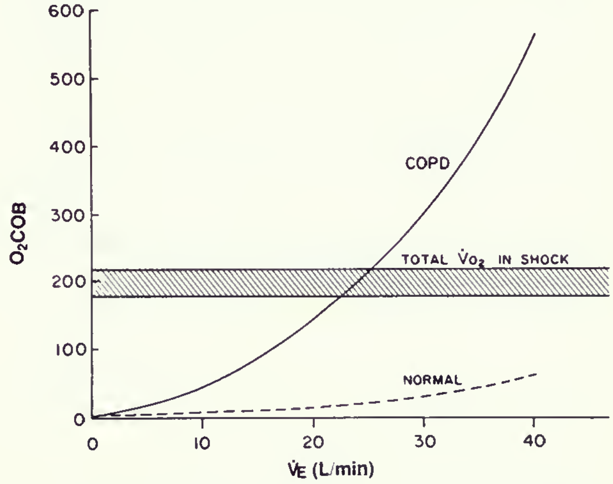


Fig. 1. Oxygen cost of breathing (O_2COB) as a function of ventilation in normal subjects and patients with COPD. Hatched areas represent total body oxygen consumption $\dot{V}_{O_2}$ reported in patients with septic shock. (From Reference 4, with permission.)

Abbreviations Used in This Paper

COPD	— Chronic obstructive pulmonary disease
EMG	— Electromyographic
F_{IO_2}	— Fractional concentration of inspired oxygen
MVV	— Maximum voluntary ventilation
O_2COB	— Oxygen cost of breathing
P_{aCO_2}	— Arterial carbon dioxide tension
P_{di}	— Transdiaphragmatic pressure
$P_{di\text{-}max}$	— Maximal transdiaphragmatic pressure
$\dot{Q}_{di}$	— Diaphragmatic blood flow
r	— Radius of curvature
t_i	— Inspiratory time
t_i/t_{tot}	— Duty cycle, or ratio of inspiratory time to total-breathing-cycle time
t_{lim}	— Inspiratory muscle endurance time
T_{tang}	— Tangential tension
t_{tot}	— Total breathing time
TT_{di}	— Tension-time index
$\dot{V}_E$	— Minute ventilation
$\dot{V}_{O_2}$	— Oxygen consumption
WOB	— Work of breathing

minute ventilation ($\dot{V}_E$) in COPD and may reach a point in which the O_2COB outstrips the total oxygen consumption ($\dot{V}_{O_2}$, 200 to 250 mL/min), a circumstance in which respiratory muscle failure becomes imminent.

On the basis of extensive studies of diaphragm function in animals, normal human subjects, and patients, several limiting conditions in diaphragm contraction have been defined (Table 3). Figure 2 depicts the relationship between $\dot{V}_E$ and endurance time, emphasizing that inspiratory muscle activity can be sustained for long periods (> 15 minutes) as long as $\dot{V}_E$ demands remain less than 60% of the maximal voluntary ventilation (MVV).[12,13] Figure 3 depicts the relationship between transdiaph-

Table 3. Conditions that Limit Diaphragm Contraction and Lead to Fatigue*

Minute ventilation > 60% of maximal voluntary ventilation
Inspiratory mouth pressure > 60% of maximal transdiaphragmatic pressure ($P_{di\ max}$)
Transdiaphragmatic pressure > 40% of $P_{di\ max}$
Tension-time index > 0.15-0.20

*Adapted from Reference 15, with permission.

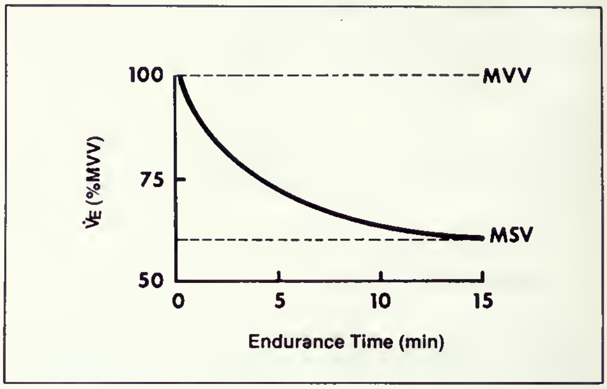


Fig. 2. Respiratory muscle endurance capacity. MVV refers to maximum voluntary ventilation for 15 seconds; MSV indicates the maximum sustainable ventilation for 15 minutes. Ventilation can be sustained for prolonged periods (> 15 minutes) as long as minute ventilation is below 60% of MVV. (From Reference 13, with permission.)

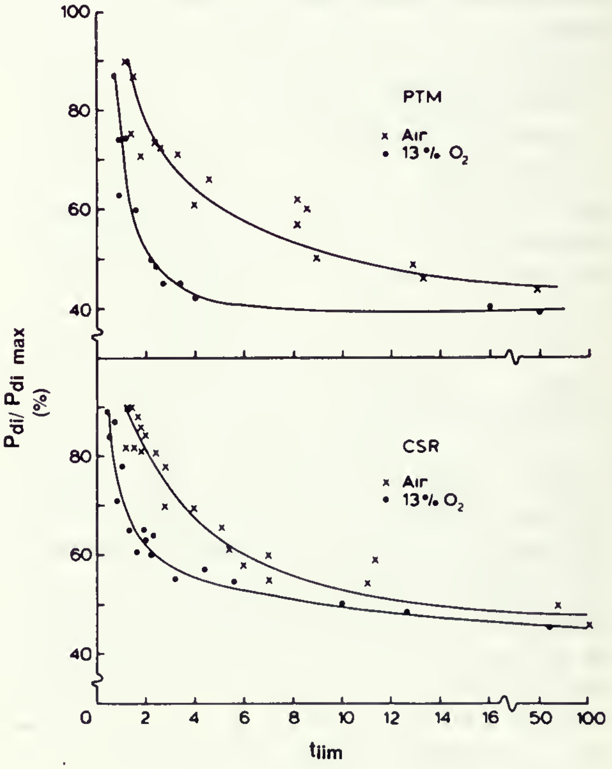


Fig. 3. Data from two patients (PTM & CSR) showing endurance time (t_{lim}) of diaphragm as function of transdiaphragmatic pressure (P_{di}) developed during each inspiration and expressed as fraction of maximum inspiratory P_{di} that can be developed at FRC ($P_{di}/P_{di\ max}$ %). Crosses indicate data obtained while breathing air; closed circles represent data obtained while breathing 13% O_2. (From Reference 12, with permission.)

ragmatic pressure (P_{di}) and inspiratory muscle endurance time (t_{lim}) and shows that inspiratory muscle function can be sustained for at least 40 minutes as long as the ratio of P_{di} to maximal transdiaphragmatic pressure ($P_{di\,max}$) is < 0.40.[12] As evidence of the dependence of diaphragmatic function on oxygen supply, diaphragmatic fatigue occurs sooner under hypoxemic conditions ($F_{IO_2} = 0.13$), although the limiting ratio of $P_{di}/P_{di\,max}$ (0.40) remains the same.[12]

Based on work by Bellemare and colleagues,[14-16] the tension-time index (TT_{di}) provides a unifying concept for defining inspiratory muscle fatigue. Recognizing that diaphragmatic fatigue is likely when the strength of contraction is high and when the duration of contraction is long, the TT_{di} reflects the product of contractile force ($P_{di}/P_{di\,max}$) and contractile duration (duty cycle, defined as ratio of inspiratory time to total-breathing-cycle time [t_i/t_{tot}]). As depicted in Figure 4, inspiratory muscle fatigue is deemed imminent when the TT_{di} exceeds 0.15. Notably, the same relationship between TT_{di} and diaphragmatic fatigue applies in normal subjects and in patients with COPD.[17] Further support for the TT_{di} comes from the observation that diaphragmatic perfusion decreases as the TT_{di} exceeds a fatiguing threshold of 0.15 (Fig. 5).[15]

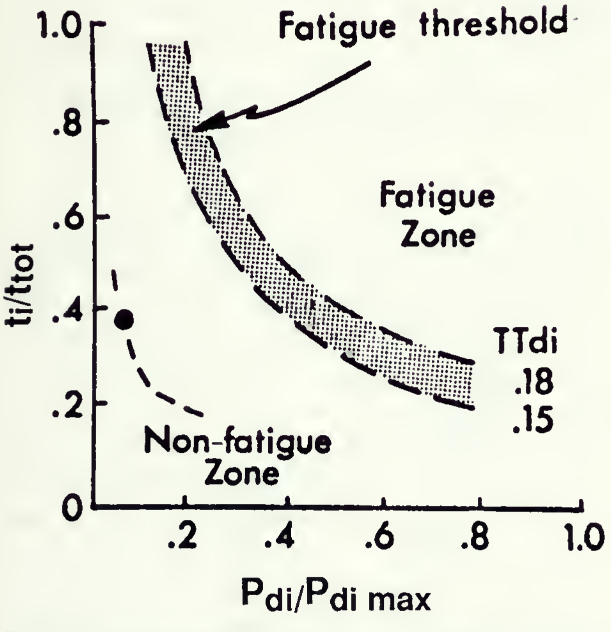


Fig. 4. The tension-time index (TT_{di}). Relation between inspiratory time (t_i/t_{tot}) and mean transdiaphragmatic pressure (P_{di}) expressed as a percentage of maximal P_{di}. Solid circle denotes breathing pattern during resting breathing. Fatigue threshold denotes breathing patterns that can be sustained for 45 minutes or longer. Fatigue zone denotes breathing patterns in which respiratory muscle fatigue becomes imminent in less than 1 hour. (From Reference 16, with permission.)

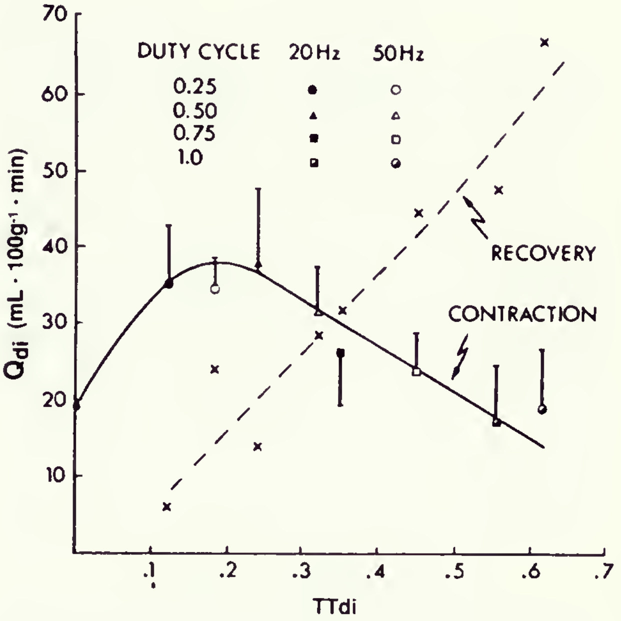


Fig. 5. Relationship between final diaphragmatic blood flow ($\dot{Q}_{di}$) during a contraction period (—), debt measured during recovery (x————x), and diaphragmatic tension-time index (TT_{di}) in 4 animals during periodic contractions with duty cycles of 0.25, 0.5, 0.75, and 1.0. Diaphragmatic blood flow diminishes at fatiguing levels of TT_{di}. (From Reference 15, with permission.)

Another property of muscle is that the force that can be generated is maximal when the muscle is close to its normal resting length.[18] Deviation from this resting length (as by stretching of the muscle) lessens its ability to generate pressure. Diaphragmatic stretching occurs with hyperinflation, and the relationship between the degree of hyperinflation and pressure generation is summarized by La Place's law (Fig. 6):

$$P = \frac{2T_{tang}}{r},$$

where P = pressure generated, T_{tang} = tangential tension, and r = radius of curvature. With hyperinflation, the radius of curvature of the diaphragm

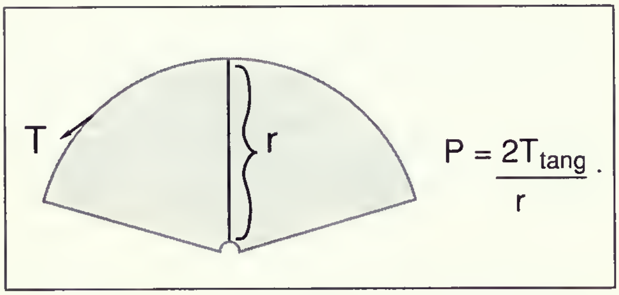


Fig. 6. LaPlace' s law applied to the diaphragm. As the chest becomes hyperinflated, the radius of curvature (r) increases and the pressure that can be generated by the diaphragm diminishes. T_{tang} = tangential tension.

increases, lessening the diaphragm's ability to generate a pressure gradient between the chest and the abdomen. On examination, Hoover's sign is a physical manifestation of diaphragmatic hyperinflation, characterized by dimpling of the chest wall inward with inspiration, reflecting the medial contraction (rather than vertical descent) of a stretched diaphragm.[19]

Evidence that Inspiratory Muscle Fatigue Can Mediate Failure To Wean

Several lines of evidence suggest that inspiratory muscle fatigue presages hypercapnia and failure to wean:

- Electromyographic (EMG) and clinical evidence of diaphragm dysfunction precedes the development of hypercapnia in patients during failed weaning attempts.[20]
- The pattern of breathing distinguishes patients who fail to wean from those who successfully discontinue mechanical ventilation.[21]
- Correlates of nonweanability include increased WOB and increased O_2COB.[7,22-30]

As observed by Cohen et al,[20] Figure 7 depicts the sequence of events observed as inspiratory muscle fatigue develops in patients who fail weaning trials. Studying 12 hypercapnic patients on mechanical ventilators, these investigators observed an early rise in respiratory rate as EMG manifestations of muscle fatigue (ie, fall in the high-low power spectrum to below 80% of baseline) developed. Dyscoordinate respiratory movements followed, characterized by respiratory alternans (alternating rib-cage and abdominal inspiratory efforts) and by abdominal paradox (inward motion of the abdominal wall during inspiration), reflecting inspiratory fall in pleural pressure transmitted across a flaccid diaphragm. Progressive hypercapnia followed these events.

Tobin et al[21] have suggested that diaphragmatic fatigue mediates weaning failure, observing that the development of rapid, shallow, spontaneous breathing distinguished patients who failed weaning trials from those who succeeded. Specifically, in a study of 17 ventilated patients undergoing weaning attempts after their maximum inspiratory pressure surpassed 20 cm H_2O, Tobin and colleagues

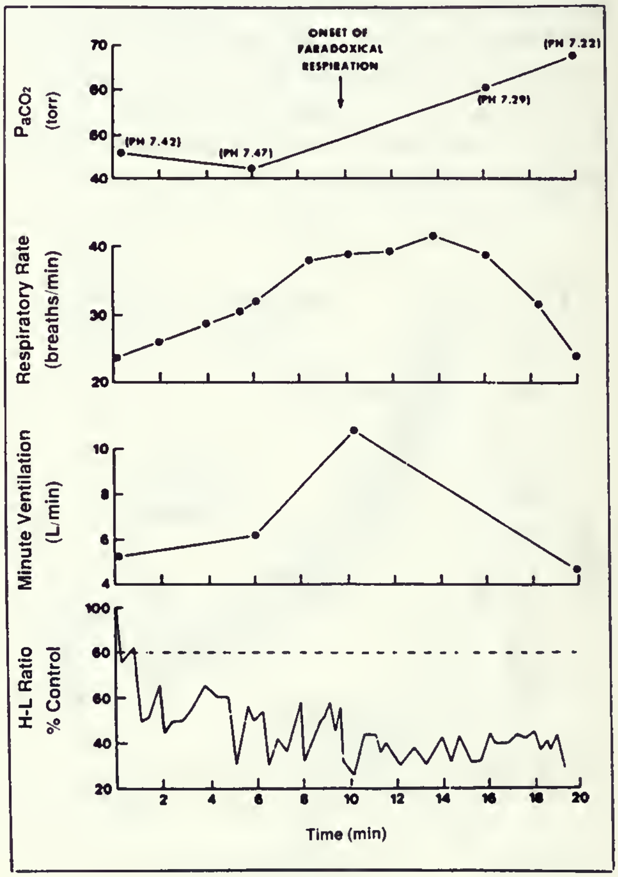


Fig. 7. Sequence of changes in P_{aCO_2}, respiratory rate, minute ventilation, and high-low ratio (H:L) of the diaphragm in a patient during a 20-minute failed weaning attempt. Paradoxic abdominal motions were not noted until after an increase in respiratory rate and minute ventilation had occurred. Hypercapnia and respiratory acidosis did not develop until after abdominal paradox and alteration between rib-cage and abdominal breaths were noted. (From Reference 20, with permission.)

observed that patients who successfully weaned sustained their tidal volume and (low) respiratory rate. In contrast, patients who failed to wean developed rapid and shallow breathing soon after beginning to breathe spontaneously.

Another line of evidence linking nonweanability and inspiratory muscle fatigue is that measures of increasing respiratory muscle work load (ie, increased WOB and O_2COB) correlate with the likelihood of weaning failure. Tables 7 and 9 in an earlier paper in this symposium[7] summarize available studies examining the relationship between transpulmonary WOB and weaning and O_2COB and weaning. Although neither WOB nor O_2COB provides a precise cut point for predicting nonweanability, and although studies examining the O_2COB are divided in their conclusions, accumulating data suggest that increasing WOB and increasing O_2COB diminish the likelihood of successful weaning.[22-30] To the extent that these correlations reflect the diaphragm's inability to meet imposed work loads, diminishing the imposed work load by resting the diaphragm remains an appealing strategy to enhance ventilation and weaning from mechanical ventilation.

Evidence that Mechanical Ventilation Can Rest the Ventilatory Muscles

In view of available evidence that ventilatory muscle fatigue can mediate respiratory failure and failure to wean, mechanical ventilation is appealing to the extent to which it rests the ventilatory muscles. Ventilatory muscle rest by mechanical ventilation has been shown by several investigators. In an early study by Rochester et al,[31] 11 chronically hypercapnic patients (mean P_{aCO_2} 59 torr) underwent negative-pressure ventilation in a tank ventilator, with EMG measurements of diaphragm and accessory muscle activity. Tank ventilation was associated with improved ventilation (P_{aCO_2} decreased to 55 torr) along with increases in diaphragm and accessory muscle EMG activity to 10.3% and 36% above baseline, respectively. Subsequent study has confirmed these observations.[32] The relative efficacies of positive- vs negative-pressure ventilation for unloading the respiratory muscles has recently been examined by Belman et al.[33] During 15-minute intervals of positive- and negative-pressure ventilation in naive normal subjects (n = 5) and normocapnic COPD patients (n = 6), these investigators observed greater reduction of diaphragmatic EMG activity and transdiaphragmatic pressures and pressure-time integral of the diaphragm with positive-pressure ventilation (nasal CPAP mask with a volume-cycled ventilator) than with negative-pressure ventilation (pneumowrap).

In summary, the optimal ventilatory mode for resting the inspiratory muscles continues to be investigated, and the conclusion that mechanical ventilation can rest inspiratory muscles seems secure. Coupled with the idea that respiratory failure reflects ventilatory muscle fatigue, this observation provides the rationale for providing mechanical ventilation to rest the inspiratory muscles. The final justification of this approach rests in the empiric observation that intermittent mechanical ventilation can enhance ventilation and ventilatory muscle function between episodes of mechanical ventilation in patients with neuromuscular disease, kyphoscoliosis, and chronic obstructive pulmonary disease. This evidence, which provides the final line of evidence rationalizing ventilatory muscle rest in hypercapnic patients, has been reviewed recently[34] and in the current symposium.[35]

REFERENCES

1. Report of the Respiratory Muscle Fatigue Workshop Group. Respiratory muscle fatigue. Am Rev Respir Dis 1990;142:474-480.
2. Belman MJ, Sieck GC. The ventilatory muscles: Fatigue, endurance, and training. Chest 1982;82:761-766.
3. Lieberman DA, Faulkner JA, Craig AB, Maxwell LC. Performance and histochemical composition of the guinea pig and human diaphragm. J Appl Physiol 1973;34:233-237.
4. Macklem PT. The vital pump. Chest 1980;78:753-758.
5. Bergofsky EH, Turino GM, Fishman AP. Cardiorespiratory failure in kyphoscoliosis. Medicine 1959;38:263-317.
6. Sharp JT, Henry JP, Sweany SK, et al. The total work of breathing in normal and obese men. J Clin Invest 1964;43:728-739.
7. Stoller JK. Establishing clinical unweanability. Respir Care 1991;36:186-198.
8. Fritts HW, Filler J, Fishman AP, Cournand A. The efficiency of ventilation during voluntary hyperpnea: Studies in normal subjects and in dyspneic patients with either chronic pulmonary emphysema or obesity. J Clin Invest 1959;38:1339-1348.

9. McIlroy MB, Christie RV. The work of breathing in emphysema. Clin Sci 1954;13:147-154.
10. McGregor M, Becklake MR. The relationship of oxygen cost of breathing to respiratory mechanical work and respiratory force. J Clin Invest 1961;40:970-980.
11. Cherniack RM. The oxygen consumption and efficiency of the respiratory muscles in health and emphysema. J Clin Invest 1959;38:494-499.
12. Roussos CS, Macklem PT. Diaphragmatic fatigue in man. J Appl Physiol 1977;43:189-197.
13. Rochester DA, Braun NMT. The respiratory muscles. Basics of RD 1978;6:1-6.
14. Bellemare F, Grassino A. Effect of pressure and timing of contraction on human diaphragmatic fatigue. J Appl Physiol 1982;53:1190-1195.
15. Bellemare F, Wight D, Lavigne CM, Grassino A. Effect of tension and timing of contraction on the blood flow of the diaphragm. J Appl Physiol 1983;54:1597-1606.
16. Grassino A, Macklem PT. Respiratory muscle fatigue and ventilatory failure. Ann Rev Med 1984;35:625-647.
17. Bellemare F, Grassino A. Force reserve of the diaphragm in COPD. J Appl Physiol 1983;55:8-15.
18. Tobin MJ. Respiratory muscles in disease. Clin Chest Med 1988;9:263-286.
19. Hoover CF. The diagnostic significance of inspiratory movements of the costal margins. Am J Med Sci 1920;159:633-646.
20. Cohen CA, Zagelbaum G, Gross D, Roussos C, Macklem PT. Clinical manifestations of inspiratory muscle fatigue. Am J Med 1982;73:308-316.
21. Tobin MJ, Perez W, Guenther SW, et al. The pattern of breathing during successful and unsuccessful trials of weaning from mechanical ventilation. Am Rev Respir Dis 1987;135:1320-1328.
22. Nishimura M, Taenaka N, Takejawa J. Oxygen cost of breathing and inspiratory work of ventilator as weaning monitor in critically ill (abstract). Crit Care Med 1984;12:258.
23. Harpin RP, Baker JP, Downer JP, Whitewell J, Gallacher WN. Correlation of the oxygen cost of breathing and length of weaning from mechanical ventilation. Crit Care Med 1987;15:807-812.
24. McDonald NJ, Lavelle P, Gallacher WN, Harpin RP. Use of the oxygen cost of breathing as an index of weaning ability from mechanical ventilation. Intensive Care Med 1988;14:50-54.
25. Shikora SA, Bistrian BR, Borlase BC, Blackborn GL, Stone MD, Benotti PN. Work of breathing: Reliable predictor of weaning and extubation. Crit Care Med 1990;18:157-162.
26. Peters RM, Hilberman M, Hogan JS, Crawford DA. Objective indications for respiratory therapy in post-trauma and post-operative patients. Am J Surg 1972;124:262-269.
27. Proctor HJ, Woolson R. Prediction of respiratory muscle fatigue by measurements of the work of breathing. Surg Gynecol Obstet 1973;136:367-370.
28. Henning RJ, Shubin H, Weil MH. The measurement of the work of breathing for the clinical assessment of ventilator dependence. Crit Care Med 1977;5:264-268.
29. Fiastro JF, Habib MP, Shon BY, Campbell SC. Comparison of standard weaning parameters and the mechanical work of breathing in mechanically ventilated patients. Chest 1988;94:232-238.
30. Brochard L, Harf A, Lorino H, Lemaire F. Inspiratory pressure support prevents diaphragmatic fatigue during weaning from mechanical ventilation. Am Rev Respir Dis 1989;139:513-521.
31. Rochester DF, Braun NMT, Lane S. Diaphragmatic energy expenditure in chronic respiratory failure: The effect of assisted ventilation with body respirators. Am J Med 1977;63:223-232.
32. Nava S, Ambrosino N, Zocchi L, Rampulla C. Diaphragmatic rest during negative pressure ventilation by Pneumowrap: Assessment in normal and COPD patients. Chest 1990;98:857-865.
33. Belman MJ, Hoo GW, Kuei JH, Shadmehr R. Efficacy of positive vs negative pressure ventilation in unloading the respiratory muscles. Chest 1990;98:850-856.
34. Levin S, Henson D, Levy S. Respiratory muscle rest therapy. Clin Chest Med 1988;9:297-309.
35. Goldstein R, Avendano MA. Long-term mechanical ventilation as elective therapy: Clinical status and future prospects. Respir Care 1991;36:297-304.

Long-Term Mechanical Ventilation as Elective Therapy: Clinical Status and Future Prospects

Roger S Goldstein MB ChB and Monica A Avendano MD

Introduction

Patients with chronic hypercapnic respiratory failure consequent to nonobstructive ventilatory disease, especially restrictive thoracic and neuromuscular disease, are increasingly referred for respiratory rehabilitation.[1] These patients are quite different from patients with chronic airflow limitation, some of whom may have hypercapnia but many of whom do not. These patients frequently have a history of prolonged periods of stability punctuated by episodic hypercapnia in association with a respiratory infection or the administration of a respiratory depressant. When chronic hypercapnia develops, the course and progress of the patient is often one of cyclic emergency intubation and mechanical ventilation followed by weaning and a return to the community. As cardiorespiratory failure progresses, arterial blood gas (ABG) values deteriorate and disability increases. Preexistent pulmonary hypertension and cor pulmonale are aggravated by exercise and minor respiratory infections.

Coexisting alterations in central respiratory control, resulting either from adaptation to chronic hypoxia and/or hypercapnia or from dysfunction such as may follow bulbar poliomyelitis, may contribute to the development of respiratory failure. In healthy persons, sleep is accompanied by state-related changes in breathing pattern, ventilatory drive, and response to hypoxia and hypercapnia.[2] Patients with a preexisting impairment of respiratory mechanics and/or control are especially vulnerable to sleep-induced changes in ventilation.[3,4] Several reports suggest that in these patients nocturnal mechanical ventilation may reduce the frequency of acute respiratory failure and may stabilize the disease process.[5-8] This clinical improvement is associated with an improvement in daytime ABG values and an enhanced level of function during the day. Accordingly, our approach to the rehabilitation of patients in whom respiratory failure is consequent to restrictive ventilatory disease is first to stabilize the disease process by elective nocturnal mechanical ventilation and then to utilize exercise training to improve function. The following comments are taken from our experience with approximately 30 patients who have been ventilated electively and now reside in the community.

Abbreviations Used in This Paper

ABG	—Arterial blood gas
EMGdi	—Diaphragmatic electromyographic activity
IPPV	—Intermittent positive-pressure ventilation
NPV	—Negative-pressure ventilation
NREM	—Non-REM
P_{CO_2}	—Carbon dioxide tension
P_{tcCO_2}	—Transcutaneous carbon dioxide tension
REM	—Rapid eye movement
S_{pO_2}	—Oxygen saturation determined by pulse oximeter
SVC	—Slow vital capacity
SWS	—Slow-wave sleep
V_T	—Tidal volume

Dr Goldstein is Associate Professor of Medicine, University of Toronto, and Director, Respiratory Medicine, West Park Hospital; and Dr Avendano is Associate Professor of Medicine, University of Toronto, and Associate Director of Respiratory Medicine, West Park Hospital—Toronto, Ontario, Canada.

A version of this paper was presented by Dr Goldstein during the Long-Term Mechanical Ventilation Symposium at the 1990 Annual Meeting of the American Association for Respiratory Care in New Orleans, Louisiana. This paper was supported by the West Park Hospital Foundation.

Reprints: Roger S Goldstein MB ChB, Director, Respiratory Medicine West Park Hospital, 82 Buttonwood Ave, Toronto, Ontario, Canada M6M 2J5.

Table 1. Pulmonary Function Characteristics of Five Patients with Restrictive Ventilatory Failure

Patient No.	Diagnosis	Age (y)	Sex	Ht (cm)	Wt (kg)	SVC (% pred)	FEV_1 (% pred)	FEV_1/ FVC (%)	FEF_{50} (% pred)	FEF_{25} (% pred)	TLC* (% pred)	D_{LCO} (% pred)	MIP† (cm H_2O)	MEP‡ (cm H_2O)	MVV (L/min)
1	Postpolio	50	M	183	62	52	55	95	62	66	81	61	22	46	73
2	Muscular dystrophy	52	F	156	33	46	62	100	131	107	74	55	22	56	49
3	Postpolio	43	F	154	40	17	23	100	52	42	54	81	20	41	43
4	Bilateral thoraco-plasties	62	M	175	85	41	28	61	10	105	95	33	81	22	25
5	Amyotrophic lateral sclerosis	62	M	176	91	45	48	78	32	20	60	75	35	94	66
Mean (SD)		54 (8)		169 (13)	62 (26)	40 (14)	43 (17)	87 (17)	57 (46)	49 (39)	66 (11)	65 (12)	29 (8)	72 (35)	51 (19)

---

*Measured with body plethysmograph.

†Measured at residual volume.

‡Measured at TLC.

Pulmonary Function Characteristics

Table 1 summarizes the pulmonary function characteristics of 5 representative patients, all of whom required nocturnal mechanical ventilatory support.[3] As can be seen, there is a reduction in mean lung volume with appropriate flowrates for the observed lung volume and a reduction in maximum inspiratory pressure measured at residual volume. ABG and pH values for 4 representative patients of ours are shown in Table 2. The blood samples were obtained while these patients were in the supine position and spontaneously breathing room air. These patients were hypoxic on room air and in chronic hypercapnic respiratory failure.[3]

Choice of Mechanical Ventilatory Support

If the patient has a tracheostomy, intermittent positive-pressure ventilation (IPPV), using a portable volume-cycled ventilator, is the obvious approach because the ventilator can easily be attached to the tracheostomy tube. Our preference is to use an uncuffed tube, which will allow the patient to speak if the leak and inspired tidal volume (V_T) are adjusted appropriately. Because psychologic and medical problems can arise during home management of a tracheostomy, we generally teach patients self-care prior to hospital discharge. In patients without a previous tracheostomy, more choices are available—patients may try different

Table 2. Arterial Blood Gas and pH Values* before and after 8 Weeks of Nocturnal Negative-Pressure Ventilation

	Before				After			
Patient No.	pH	P_{aCO_2} (torr)	P_{aO_2} (torr)	S_{aO_2} (%)	pH (torr)	P_{aCO_2} (torr)	P_{aO_2} (torr)	S_{aO_2} (%)
Patient 1	7.40	57	49	83	7.40	43	80	95
Patient 2	7.39	54	61	89	7.37	47	68	92
Patient 3	7.39	58	44	79	7.38	48	61	89
Mean (SD) of Pts 1-3	7.39 (0.01)	56 (2)	51 (9)	84 (5)	7.38 (0.02)	46 (3)†	70 (10)	92 (3)†
Patient 4	7.33	81	65	89	7.40	55	66	92

---

*All blood samples were obtained in the afternoon with patients in the supine position and spontaneously breathing room air, except Patient 4 who was receiving nasal oxygen at 2 L/min.

†Significantly different from Before value, $p < 0.05$.

mechanical ventilation devices (eg, IPPV by nasal mask or negative-pressure ventilation [NPV] by chest cuirass), choosing the most comfortable and appropriate for their home environment.

Because fatigue of the inspiratory muscles is thought to be a contributing factor in the development of respiratory failure, the influence of mechanical support on electromyographic activity has been studied. Figure 1 shows the diaphragmatic electromyogram (EMGdi) of a patient who wished to try both a rocking bed and a chest cuirass negative-pressure ventilator.[9]

During unassisted breathing, the EMGdi can be seen clearly and is synchronous with the excursion of the rib cage and abdomen, denoting tidal breathing. During use of the rocking bed, the EMGdi is still quite evident. During use of the chest cuirass, the EMGdi is attenuated in the presence of regular excursions of the rib cage and abdomen.

Figure 2 compares the effect of ventilatory support provided by rocking bed and chest cuirass on V_T, oxygen saturation determined by pulse oximeter (S_{pO_2}), and transcutaneous P_{CO_2} (P_{tcCO_2}) in a group of 7 patients in respiratory failure resulting from restrictive disease.[9] Note that whereas both methods improved V_T, negative-pressure ventilation resulted in a greater reduction in P_{tcCO_2} than did the rocking bed.

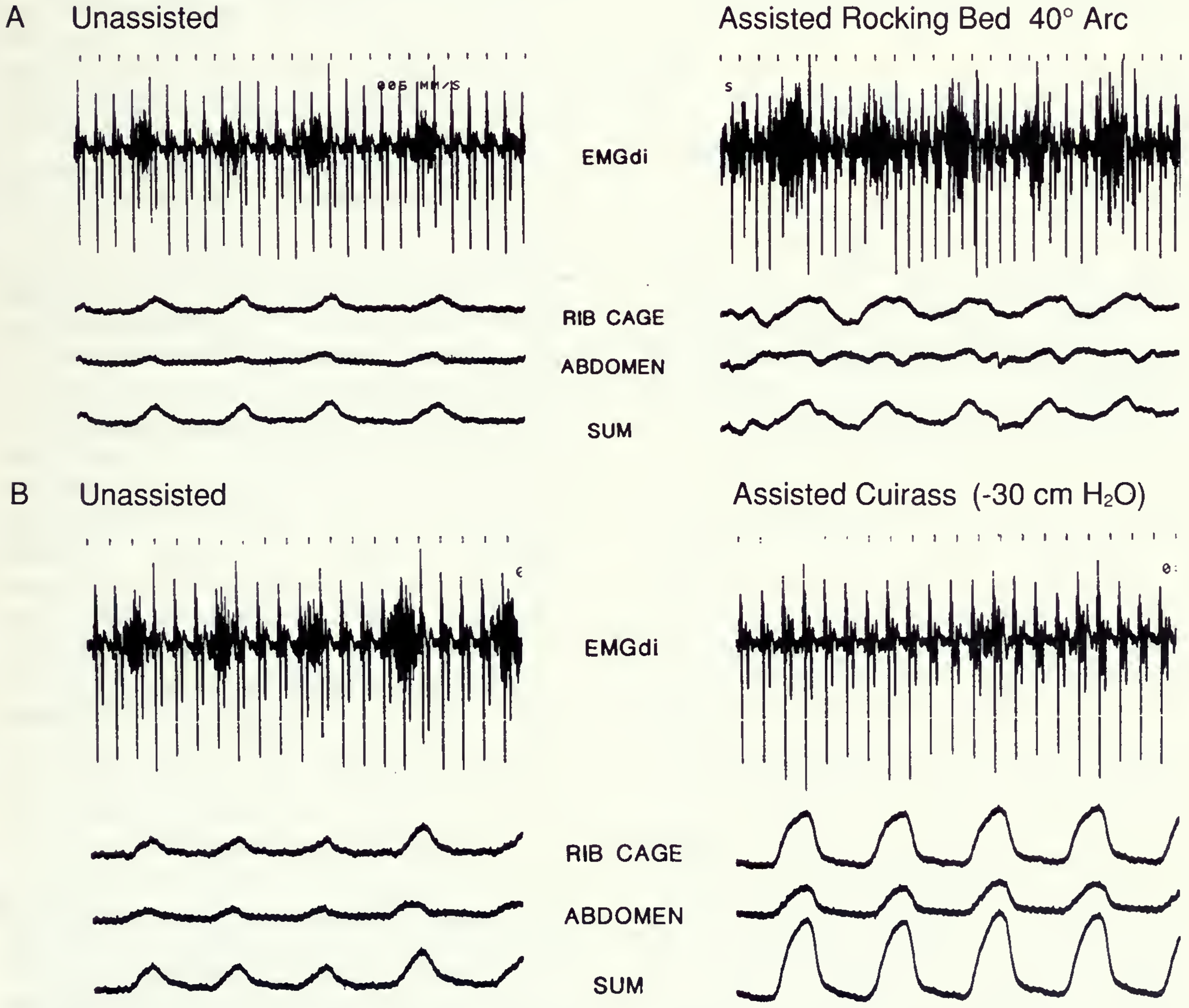


Fig. 1. Recording of diaphragmatic electromyographic activity (EMGdi) from an esophageal electrode during: A—unassisted breathing and ventilatory support by rocking bed (RB) and B—unassisted breathing and negative-pressure ventilation (NPV) by chest cuirass. Note the attenuation of electrical activity during NPV compared to RB.

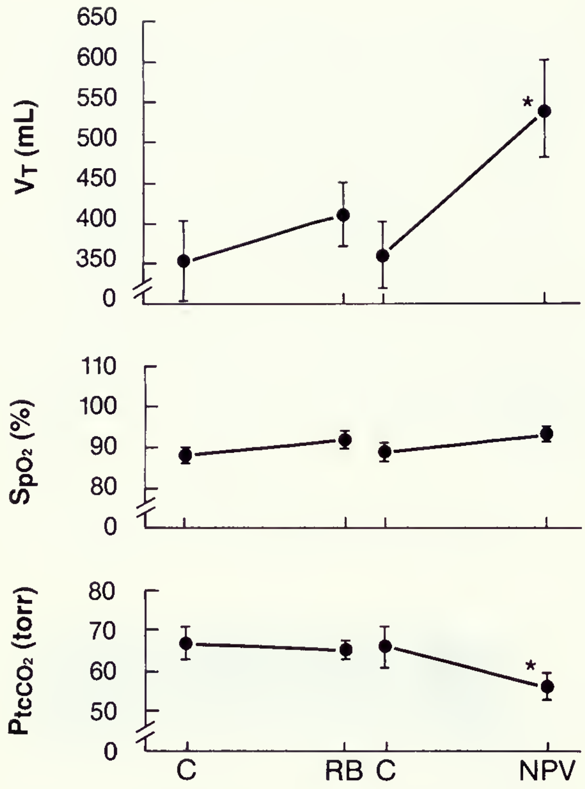


Fig. 2. Mean (SD) effect of ventilatory support provided by rocking bed (RB) and negative pressure ventilation (NPV) on V_T, S_{pO_2}, and P_{tcCO_2} in 7 patients. C denotes mean (SD) control values for V_T, S_{pO_2}, and P_{tcCO_2} measured during unassisted ventilation. Note greater V_T and lower P_{tcCO_2} with NPV compared to RB, $p < 0.05$.

Figure 3 shows recorder tracings from a sleep study of a 50-year-old man who presented in hypercapnic respiratory failure.[3] At age 19, he had been ventilated by tank respirator for 5 months because of respiratory poliomyelitis. Subsequently, for 30 years, he had been stable without respiratory problems. At the time of the sleep study, his resting oxygen saturation could be improved with supplemental oxygen but marked hypercapnia resulted. At night his P_{tcCO_2} regularly reached 90-100 torr [12-13 kPa]. During sleep, spontaneous room-air breathing resulted in a rapid and shallow breathing pattern. During rapid-eye-movement (REM) sleep, further decreases occurred in rib-cage and abdominal excursion, and oxygen saturation fell progressively. During sleep, with NPV, V_T increased and S_{pO_2} remained close to 95%. During REM sleep there appeared to be paradoxical movement between the rib cage and the abdomen, which terminated in an arousal.

In a group of 5 similar patients S_{pO_2} and P_{tcCO_2} were monitored (Fig. 4) during wakefulness, non-REM (NREM) sleep, and REM sleep, during unassisted ventilation (on the control night prior to initiating nocturnal assisted ventilation), assisted ventilation, and unassisted ventilation (on the first night after 8 weeks of nocturnal assisted ventilation). Nocturnal gas exchange deteriorated as soon as the ventilator was withdrawn, despite previous maintenance of normal ABG values each night for 8 weeks with nocturnal assisted ventilation. Irrespective of the type of nocturnal mechanical ventilation used, daytime ABG values improved (Table 2). Daytime functioning also improved and patients were often able to return to work. In our rehabilitation program, we usually combine nocturnal assisted ventilation with daytime supervised exercise training. Table 3 shows 6-minute-walk distances for 6 patients before and after 3 months of nocturnal positive-pressure ventilation by nasal mask.

Intermittent positive-pressure ventilation via nasal mask has been reported to be effective in managing chronic respiratory failure in patients with either neuromuscular or restrictive thoracic disease.[10-13] Nocturnal nasal-mask ventilation has been observed to be capable of maintaining an adequate arterial oxyhemoglobin saturation during sleep and of improving ABG values during the day. It may be more effective than NPV, and certainly avoids the complication of upper-airway obstruction associated with NPV. The improvement in nocturnal gas exchange, daytime function, and daytime ABG values has been associated with an improvement in inspiratory muscle endurance sustained at 3 months.[10] Figure 5 shows recorder tracings from a sleep study of a patient with kyphoscoliosis. During sleep, spontaneous breathing with 2 L/min nasal oxygen resulted in a rapid and shallow breathing pattern with little rib-cage excursion. During REM sleep, there were further reductions in rib-cage and abdominal excursion, resulting in hypoventilation to the point of central apnea.[10] During wakefulness, slow-wave sleep (SWS), and REM sleep, intermittent positive-pressure room-air ventilation by nasal mask resulted in stable S_{pO_2} close to 95% and increased V_T compared to that monitored on the control night.

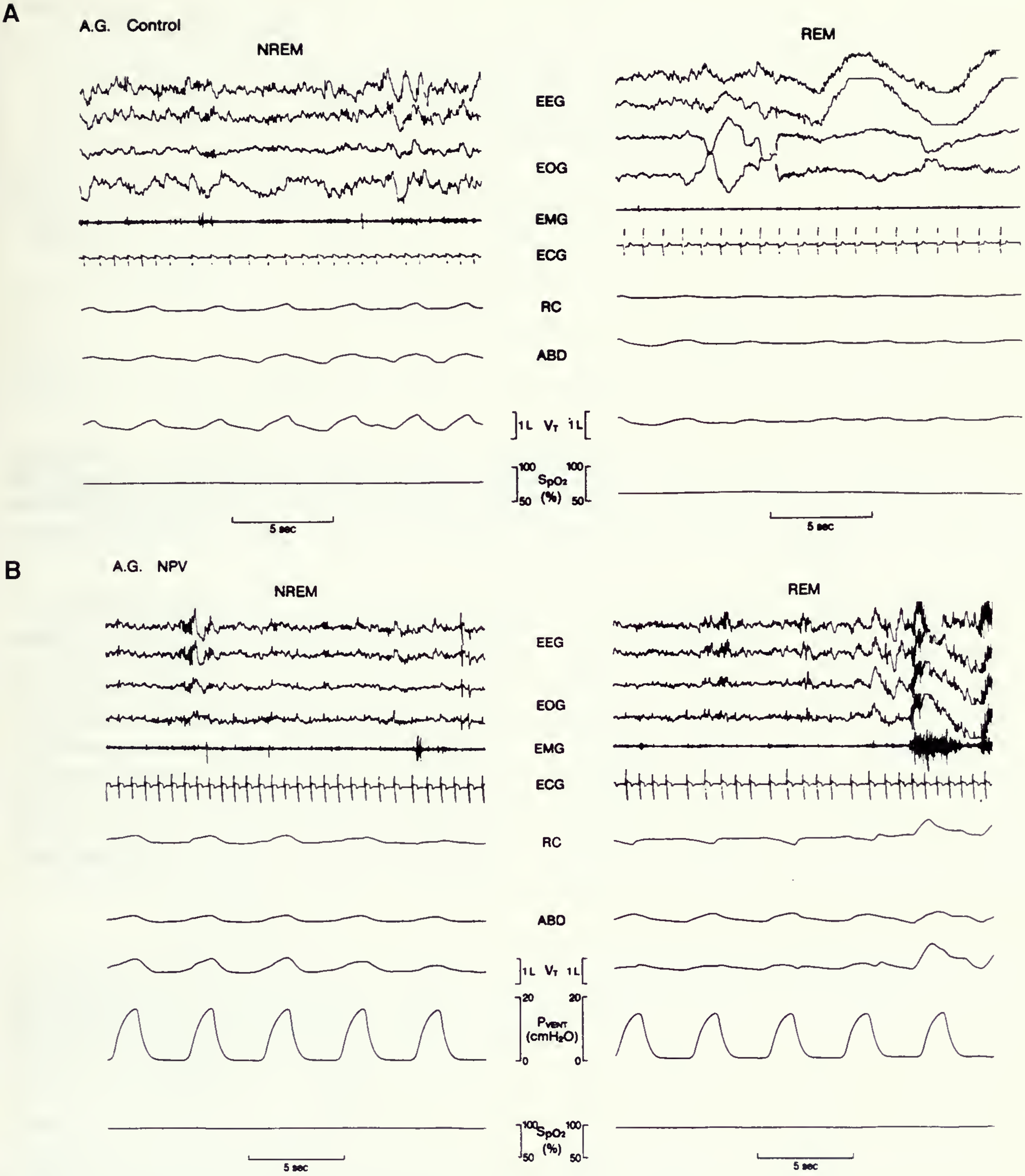


Fig. 3. Recorder tracings from a patient with postpoliomyelitis: A—During NREM sleep, spontaneous room-air breathing resulted in a rapid and shallow breathing pattern; during REM sleep, S_{pO_2} decreased further. B—During NREM sleep, negative-pressure room-air ventilation resulted in increased V_T and stable S_{pO_2} close to 95%; during REM sleep, paradoxical movement between abdomen and rib cage terminated in an arousal. Abbreviations from top to bottom: electroencephalogram (EEG); electroocculogram (EOG); submental electromyogram (EMG); electrocardiogram (ECG); excursion of the rib cage (RC), excursion of the abdomen (ABD), and sum of excursions (VT).

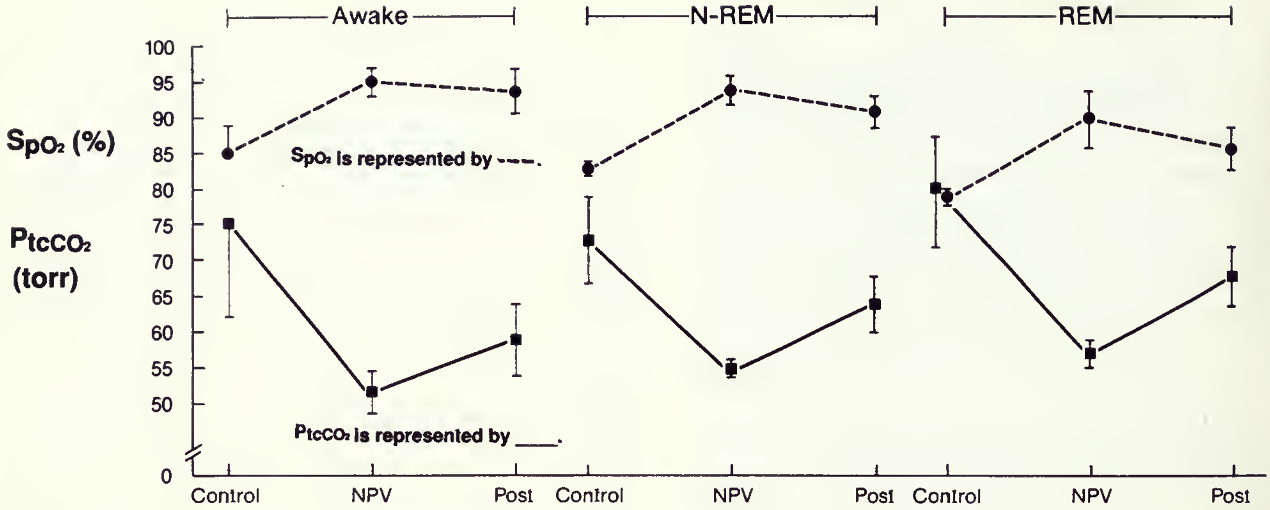


Fig. 4. In a group of 5 similar patients S_{pO_2} and P_{tcCO_2} were monitored during wakefulness, NREM sleep, and REM sleep, during unassisted ventilation (on the control night prior to initiating nocturnal assisted ventilation), assisted ventilation, and unassisted ventilation (on the first night after 8 weeks of nocturnal assisted ventilation). Nocturnal gas exchange deteriorated as soon as the ventilator was withdrawn, despite previous maintenance of normal ABG values each night for 8 weeks with nocturnal assisted ventilation.

Criteria for Elective Ventilation

It is important to establish clear criteria for mechanical ventilation. Prospective controlled studies are needed to confirm appropriate selection criteria and to delineate the influence of early elective ventilation on quality of life, morbidity, mortality, and cost of health care. Criteria for elective ventilation might include diagnosis of respiratory failure consequent to nonobstructive ventilatory impairment, clinical history of stability punctuated by episodic acute respiratory failure requiring emergency ventilatory support, or a history of progressive deterioration with symptoms suggestive of sleep-related alterations in gas exchange. Although elective nocturnal ventilation may play an important role in the management of such patients, it remains to be determined at what level of arterial P_{CO_2} ventilation should be introduced and what measurements of pulmonary mechanics should be made to help the clinician make this decision. Obviously, one of the objectives of elective ventilation is to avoid emergency intubation and mechanical ventilation.

Table 3. Comparison of 6-Minute-Walk Distances* in Patients with Restrictive Ventilatory Failure, before and after 3 Months of Nocturnal Positive-Pressure Nasal-Mask Ventilation

Patient No.	Before	After
1	500	723
2	294	418
3	586	641
4	438	570
5	329	559
6	411	559
Mean (SD)	426 (108)	566 (108)

*6-minute-walk distances measured in meters.

Home Training

Patients will only comply with mechanical ventilation if adequate patient and family education has been provided. In our unit, this education is coordinated by a nurse and a respiratory therapist; group teaching sessions are provided on a weekly basis and individual sessions are provided to meet the special needs of each patient. Because chronic illness imposes psychosocial stress on both patients and their families, psychosocial support must be provided. Relaxation training should be made available to the patient, and both the patient and family members should be encouraged to participate in multidisciplinary team conferences.[14] To facilitate

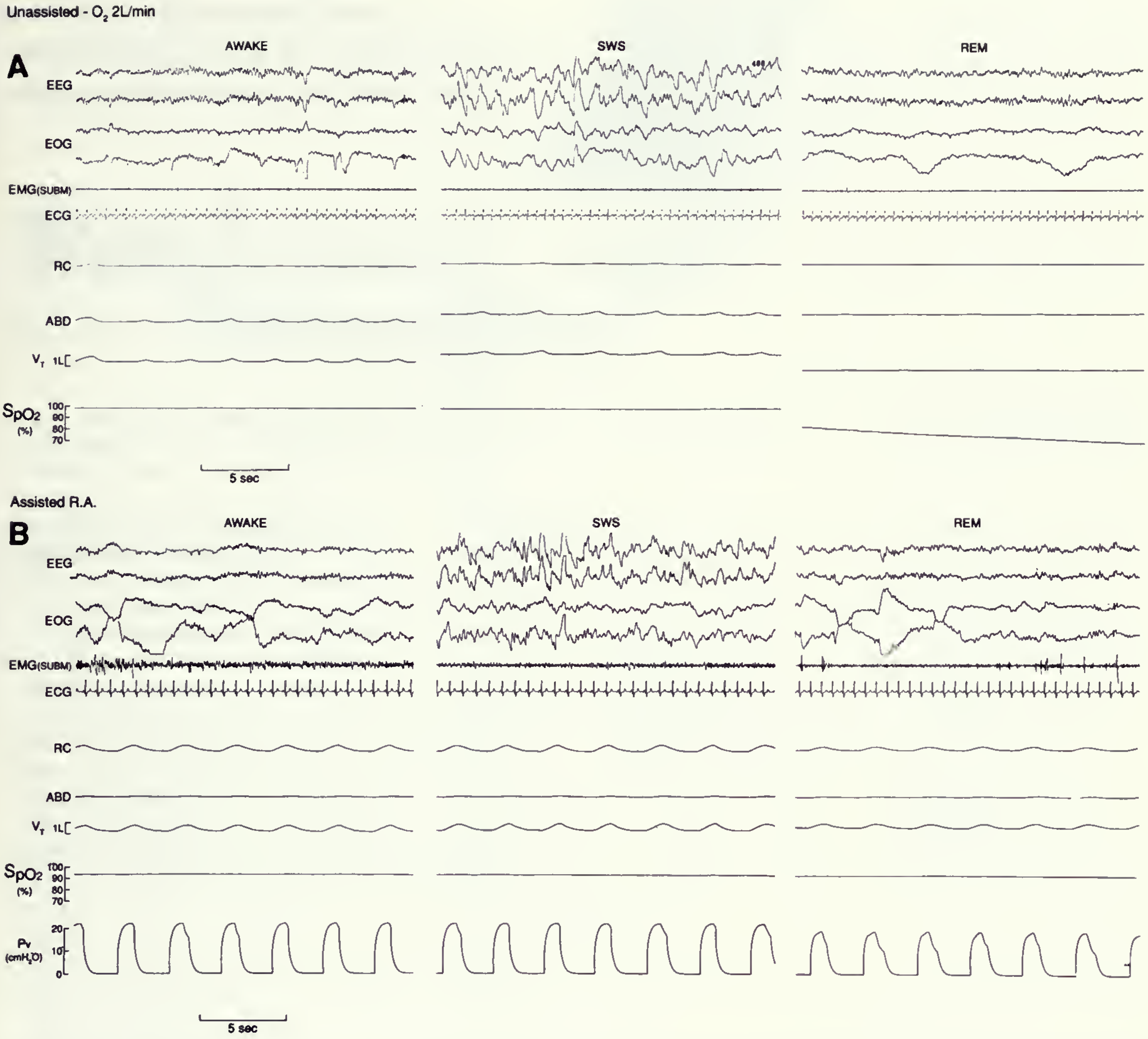


Fig. 5. Recorder tracings from a patient with kyphoscoliosis: A—during slow-wave sleep (SWS), spontaneous breathing with supplemental nasal oxygen resulted in rapid and shallow breathing pattern; during REM sleep, rib-cage and abdominal excursion resulted in hypoventilation to the point of central apnea. B—during wakefulness, slow-wave sleep, and REM sleep, intermittent positive-pressure room-air ventilation by face mask resulted in stable S_{pO_2} close to 95% and increased V_T compared to that monitored during the control night.

a smooth transition between hospital and home, a progressive discharge schedule should be implemented early in the management of the patient, with at least a 1-weekend trial at home prior to the final discharge.

Follow-up is necessary on a regular basis. Our practice is to admit patients for a full assessment 8 weeks after they return to the community and annually thereafter. In our assessment, we evaluate the patient's daytime functional performance, nocturnal gas exchange, and understanding of the ventilator.

Conclusion

In conclusion, rehabilitation of patients with respiratory failure consequent to restrictive ventilatory disease can include elective mechanical ventilation when the clinical presentation suggests that the patient is progressively deteriorating. Noninvasive, elective mechanical ventilation can be established in the setting of a respiratory rehabilitation centre, thus avoiding the need for hospitalization in an acute care centre. By stabilizing the disease, it is anticipated that fewer days will be spent in the hospital. Other important consequences of nocturnal ventilation are improved ABG values during the day, increased exercise tolerance, and improved functional capacity.

ACKNOWLEDGMENTS

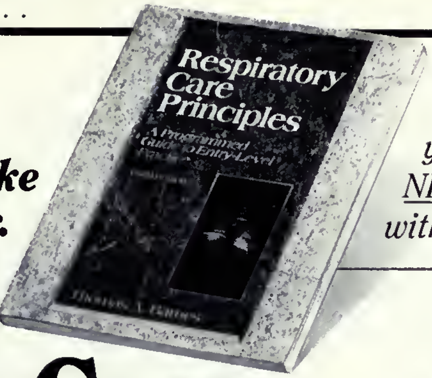
The assistance of Diane Mills in preparing the manuscript is greatly appreciated.

REFERENCES

1. Goldstein RS, McCullogh C, Avendano MA. Approaches to rehabilitation of patients with ventilatory insufficiency. Eur Respir J 1989;2:655-660.
2. Phillipson EA. Control of breathing during sleep. Am Rev Respir Dis 1978;118:909-939.
3. Goldstein RS, Molotiu N, Skrastins R, et al. Reversal of sleep-induced hypoventilation in chronic respiratory failure by nocturnal negative pressure ventilation in patients with restrictive ventilatory impairment. Am Rev Respir Dis 1987;135:1049-1055.
4. Mezzon BL, West P, Israels J, Kryger M. Sleep and breathing abnormalities in kyphoscoliosis. Am Rev Respir Dis 1980;122:617-622.
5. Garay SM, Turino GM, Goldring RM. Sustained reversal of chronic hypercapnia in patients with alveolar hypoventilation syndromes. Am J Med 1981;70:269-274.
6. Marino W, Braun NMT. Reversal of the clinical sequelae of respiratory muscle fatigue by intermittent mechanical ventilation (abstract). Am Rev Respir Dis 1982;125 (4, Part 2):85.
7. Hoeppner VH, Cockroft DW, Dosman JA, Cotton DJ. Nighttime ventilation improves respiratory failure in secondary kyphoscoliosis. Am Rev Respir Dis1984;129:240-243.
8. Rochester DF, Braun NMT, Lane S. Diaphragmatic energy expenditure in chronic respiratory failure—The effect of assistive ventilation with body respirators. Am J Med 1977;62:223-232.
9. Goldstein RS, Molotiu N, Skrastins R, Long MS, Avendano M. Assisting ventilation in respiratory failure by negative pressure ventilation and by rocking bed. Chest 1987;92:470-474.
10. Goldstein RS, De Rosie JA, Avendano MA, Dolmage TE. Influence of noninvasive positive pressure ventilation on inspiratory muscles. Chest 1991;99:408-415.
11. Segall D. Noninvasive nasal mask assisted ventilation in respiratory failure of Duchenne muscular dystrophy. Chest 1988;93:1298-1300.
12. Bach JR, Alba AS. Management of chronic alveolar hypoventilation by nasal ventilation. Chest 1990;97:52-57.
13. Ellis ER, Bye PTP, Bruderer JW, Sullivan CE. Treatment of respiratory failure during sleep in patients with neuromuscular disease. Am Rev Respir Dis 1987;135:148-152.
14. Gilmartin ME. Long-term mechanical ventilation: Patient selection and discharge planning. Respir Care 1991;36:205-216.

■ JUST PUBLISHED IN A NEW 3RD EDITION . . .

The book that makes learning the principles of respiratory care so easy, *it's like having your own private tutor.*


Respiratory Care Principles
A Programmed Guide to Entry-Level Practice

Read at your own pace to prepare yourself to pass the NBRC entry-level exam with flying colors!

Respiratory Care Principles:

A PROGRAMMED GUIDE TO ENTRY-LEVEL PRACTICE, NEW 3RD EDITION

Now published in a new, completely updated third edition, **Respiratory Care Principles: A Programmed Guide to Entry-Level Practice,** is the only programmed text covering the respiratory care field. Its flexibility and comprehensiveness make it ideal for independent study as well as for any classroom situation.

You'll want to note these important features:

- Organizes the subject into 242 instructional frames of information which you complete at your own pace
- Includes 1,040 referenced review questions which comprehensively cover the material on the NBRC entry-level exam
- Presents nine new chapters, including Assessment and Diagnosis, Airway Care, Cardiopulmonary Resuscitation, Monitoring Patient Response, Pulmonary Rehabilitation and Home Care, Oxygen Therapy Equipment, Humidity and Aerosol Equipment, Airway Equipment, and Mechanical Ventilators
- Each chapter includes pre- and post-test multiple choice and multiple true/false questions to match the type of questions on the NBRC exams
- 170 chapter exercises help you learn more about the principles covered in the text
- The final exam has been expanded from 50 to 200 questions for an even more thorough review

By **Thomas A. Barnes,** EdD, RRT,
Associate Professor of Respiratory Therapy,
Director of Clinical Education,
Respiratory Therapy Program,
College of Pharmacy and Allied Health Professions,
Northeastern University,
Boston, Massachusetts.

About 515 pp., 135 ill. Soft cover.
1991. About $35.00.

■ OTHER IMPORTANT TITLES . . . ■

The Respiratory Care Workbook

Keyed to all major textbooks, this useful workbook provides coverage from basic to advanced levels, with a strong emphasis on integrating theory and clinical application of knowledge.

By **Howard B. Surkin,** MA, RRT, and **Anna Weigand Parkman,** MBA, RRT.
372 pp. 125 ill. Soft cover.
1990. $24.95.

Respiratory Facts

Written in outline style, this pocket-sized guide gives you the maximum amount of information in the minimum number of words. Explanations are reinforced with carefully formulated tables, charts and graphs.

By **John H. Riggs,** BA, RRT.
327 pp. Illustd. Soft cover.
1989. $18.95.

Please send me the indicated titles on 30-day approval

PLEASE PRINT
Full Name ____
Address ____
City ____
State ____ Zip ____

☐ **Payment Enclosed.** We pay postage and handling. Pennsylvania residents please include 6% state sales tax.
☐ **Bill me.** An invoice, including a small charge for postage and handling, will accompany each book you order. State sales tax will be charged where appropriate.

I would like to charge my purchase through:
☐ VISA ☐ MasterCard

Signature ____
Account No. ____
Expiration Date ____

☐ 0662 Barnes: **Respiratory Care Principles: A Programmed Guide to Entry-Level Practice.** About $35.00.

☐ 8229 Surkin & Parkman: **The Respiratory Care Workbook.** $24.95.

☐ 7333 Riggs: **Respiratory Facts.** $18.95.

☐ 3491 Finucane & Santora: **Principles of Airway Management.** $21.95.

Prices are subject to change without notice.

4/91 RC

F.A. DAVIS COMPANY 1915 ARCH STREET, PHILADELPHIA, PENNSYLVANIA 19103

Circle 144 on reader service card

Drug Capsule

Hugh S Mathewson MD, Section Editor

Antiviral Agents for Prevention of the Common Cold

Hugh S Mathewson MD

Upper respiratory infections (URIs) are the most frequent acute illnesses in the industrialized world.[1] Most of them are common colds; together with influenza and other viral infections they account for roughly half of all reported acute illnesses in the United States.[2] According to a national survey URIs have an incidence rate of 31 episodes per 100 persons per year. This survey reported only those cases that received medical attention or were associated with at least one day of restricted activity.[2] Each year, Americans miss more than 100 million workdays from URIs, with a national loss of productivity estimated at 5 billion dollars annually. URIs contribute substantially to the national cost of health care; they rank second only to "general medical examinations" as causes of physician visits.[3]

However burdensome to the health care system and to the general economy, the common cold is rarely a serious illness. The clinical course is usually mild and lasts only 4 or 5 days. Complications are uncommon, and tend to occur only in the aged, debilitated, or immunosuppressed. In healthy persons, common colds are so rarely severe that experiments involving exposure to live viruses can be carried out on human volunteers. Thus, they provide a way of studying the clinical behavior of viruses in controlled settings and to test antiviral agents in a systematic fashion. Several research centers over the world are dedicated to common cold investigations. Perhaps the best known is the Medical Research Council Common Cold Unit, located in Salisbury, England.

About 30-50% of colds are caused by rhinoviruses, a class of small viruses (picornaviruses) biologically related to the enteroviruses that cause poliomyelitis and hepatitis A.[4] The name "picorna" is derived from *pico* (small) *RNA*-containing. Rhinovirus particles are about 27 nanometers in diameter, and their genes are in the form of a single strand of ribonucleic acid (RNA). About 100 different rhinoviruses, called serotypes, have been identified. Any otherwise healthy adult with cold symptoms is most likely to have a rhinovirus infection, and a succession of colds with similar symptoms is likely to result from a different rhinovirus serotype for each episode.[5]

About 15-20% of colds are caused by coronaviruses, a distinct family of RNA-containing organisms about 100 nanometers in diameter.[6] Characteristically, they affect adolescents and young adults during the winter months, particularly those in crowded environments such as school dormitories and military camps. Influenza virus infections tend to occur in epidemics; the cold symptoms are often accompanied by intense myalgias. Infants and children may have URIs caused by respiratory syncytial virus or by members of the parainfluenza family. Adenoviruses account for an appreciable number of cases, often with colds accompanied by conjunctivitis and acute bronchitis. These outbreaks are commonest among college students and military recruits.[7]

Much of the following discussion will center on rhinoviruses because many of the antiviral compounds prepared for treatment of the common cold are directed toward their inactivation. Similar to many viral families, the rhinoviruses have the RNA strand surrounded by a crystal-like protective protein shell, or capsid, which is structured in the form of a regular geometric solid, the icosahedron (Fig. 1). Mainly through a method of analysis called x-ray protein crystallography, Rossman and associates[8] have determined the precise amino acid sequence of the proteins of the icosahedral shell. With a relatively clear picture of the viral architecture, it has now become possible to examine

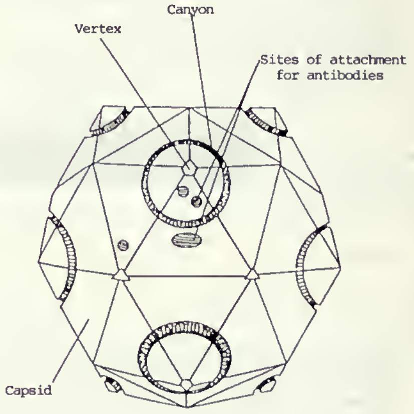


Fig. 1. Model of a rhinovirus, showing the typical icosahedral shell (modified from Reference 9).

Dr Mathewson is Professor of Anesthesiology and Medical Director, Respiratory Therapy, University of Kansas Health Sciences Center Kansas City, Kansas.

the mode of attack of the virus on the respiratory mucosa at the molecular level.

Rossman[9] has postulated that around each of the 12 icosahedral vertices runs a deep groove or 'canyon.' At the bottom of the canyon, there is a molecular structure that interacts with protruding receptors on nasal mucosal cells. When the receptors penetrate the canyon, the viral capsid opens and the RNA strand is introduced into the cell. The 100 serotypes of rhinoviruses are mainly distinguished by the variations of amino acid structure in the canyon. Antibodies to rhinovirus infections have been shown to attach to the rim of the canyon, thus interfering with interaction between the virus particles and the cell receptors.

Despite these advances in virology, progress toward the development of safe and effective antiviral agents has been slow. Several antiviral compounds that are nucleoside analogs (and thus are DNA or RNA antimetabolites) have attained clinical stature. They include acyclovir (effective against herpes simplex virus) and some related antimetabolites (effective against retroviruses) the best known of which is azidothymidine. However, such compounds interfere significantly with host cell replication, and their antiviral potency tends to parallel their activity as general cell poisons.

In 1964, amantidine, a synthetic antiviral agent, was found to be effective in preventing infections with influenza A virus. Once the disease developed, the drug had little or no therapeutic value. The mode of action of amantadine is not fully known, but there is considerable evidence that it interferes with uncoating of the virus particle, which prevents entry of the nucleoside strand into the host cell.[10]

Over the past two decades, several compounds have been shown to have a similar prophylactic effect against rhinovirus infections. The formulas of a few of them, all with high in-vitro antiviral activity, are shown in Figure 2. Beyond a certain rigidity and

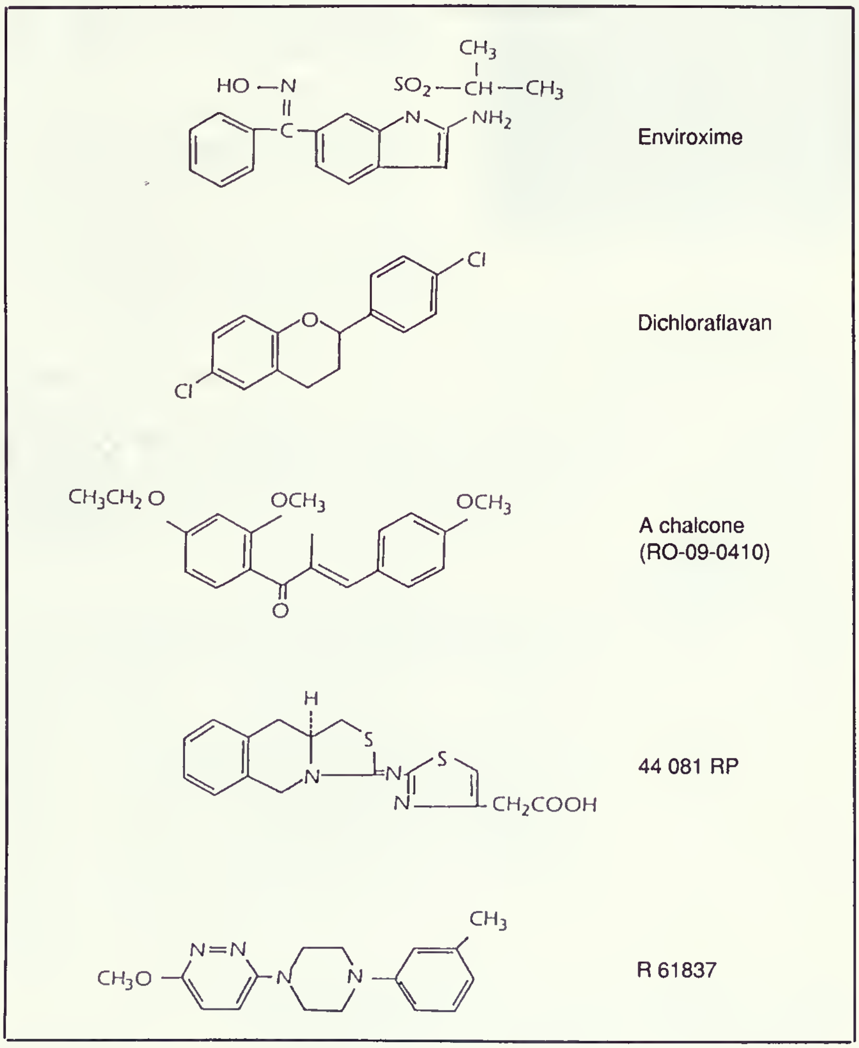


Fig. 2. Antirhinovirus compounds with similar prophylactic properties and high in-vitro, antiviral activity.

bulkiness of structure, they do not show any marked chemical similarities. Enviroxime, first tested clinically in 1982,[11] has preventive activity but no effect on established colds. Similarly, dichloroflavan showed high prophylactic action against some rhinoviruses, although certain serotypes were relatively unaffected.[12] Because it is relatively nontoxic, dichloroflavan could be given in sufficient doses to produce high plasma levels. However, administered in this manner it is ineffective, apparently because the drug does not reach the nasal epithelial cells.[13]

The chalcone, RO-09-0410, was developed by Nippon Roche from an oriental herbal remedy, and proved to be nearly valueless when given orally,[14] but had demonstrable effectiveness when given by nasal spray. The Rhone-Poulenc compound (44 081 RP) was unsuitable for oral administration, and was tested intranasally. It did not offer sufficient protection to justify extended trials.[15] These compounds, promising in vitro but disappointing clinically, were found to possess a common property; all prevented uncoating of the rhinovirus. The molecular sites of action on the capsid varied, but the stabilizing effect accomplished the same biological results.[16,17]

The strategy now appears to be to develop a molecule with high in-vitro potency and test its effectiveness by topical application. A definitely more promising compound has been synthesized at the Janssen Laboratories, R 61837.[18] Clinical trials have shown that it prevents rhinoviral colds when given by intranasal spray, but it rapidly becomes ineffective after symptoms appear. R 61837 is nearly insoluble in water, but when combined with a cyclodextrin (a cyclic carbohydrate that is water soluble) a topical preparation can be made with improved access to the nasal mucosa.[19]

It is evident that rhinoviruses are innocuous until they penetrate the mucosal cell; once entered, they must be combatted by natural immune mechanisms. Here the trials with interferon should be mentioned. Interferons are a family of glycoproteins elaborated by leukocytes and other cells, belonging to a class known collectively as cytokines. They have antiviral immunomodulating and antiproliferative effects. They can prevent protein synthesis in many viruses, but prevention of uncoating probably accounts for their major beneficial action.[20] The derivative known as interferon alpha is very effective intranasally in preventing rhinoviral colds.[21] It is of no value in treating established colds and can cause nasal irritation or bleeding. The use of human interferon has become more practical now that it can be obtained in large quantities from genetically engineered *Escherichia coli*. If in further studies interferon proves to be safe and cost-effective, it could help to reduce the spread of colds in groups of people subject to crowding and multiple exposure.

The overall lack of toxicity of the compounds just described is encouraging, and has largely countered the widely held opinions that viral replication is inseparably linked to cellular metabolism and that antiviral agents are inherently toxic.[22] The inhibition of viral uncoating appears to be a highly applicable investigative principle.[23] When this can be accomplished by topical application to the nasal mucosa, rhinoviral invasion can be effectively prevented without undue risk. However, this is chemoprophylaxis, not chemotherapy. Once a cold is established intracellularly, no drugs yet promise to eliminate the virus or promote more rapid resolution of the infection. The symptoms can be ameliorated to some degree, but the common cold will continue to be widespread until more is understood of the intracellular life cycles of viruses and the tissue responses they produce.

REFERENCES

1. Lowenstein SR, Parrino TA. Management of the common cold. Adv Intern Med 1987;32:207-234.
2. National Center for Health Statistics: Current estimates from the National Health Interview Survey, United States, 1982. Vital and Health Statistics Series 10, No. 150. U.S. Department of Health and Human Services, publication (PHS) 85-1578. Public Health Service, 1985.
3. Gold M, Azevedo D. The content of adult primary care episodes. Public Health Rep 1982;97:48-57.
4. Turner RB, Gwaltney JM. Symposium on rhinovirus pathogenesis. Acta Otolaryngol 1984;(Suppl 413):5-45.
5. Hendley JO. Rhinovirus colds: Immunology and pathogenesis. Eur J Respir Dis 1983;64(Suppl 128):340-343.
6. Gwaltney JM. Rhinovirus colds: Epidemiology, clinical characteristics and transmission. Eur J Respir Dis 1983;64(Suppl 128):336-339.
7. Anderson LJ, Patriarca PA, Hierholzer JC, Noble GR. Viral respiratory illnesses. Med Clin North Am 1983;67:1009-1030.
8. Rossmann MG, Arnold E, Erickson JW, et al. Structure of a human common cold virus and functional relationship to other picornaviruses. Nature 1985;317:145-153.
9. Rossmann MG. The canyon hypothesis: Hiding the host cell receptor attachment site on a viral surface from immune surveillance. J Biol Chem 1989;264:14587-14590.
10. Hayden FG, Douglas RG Jr. Antiviral agents. In: Mandell GL, Douglas RG Jr, Bennett JE, eds. Principles and practice of infectious diseases; 3rd ed. New York: Churchill Livingstone, 1990:359-380.
11. Phillpotts RJ, Wallace J, Tyrrell DAJ, Tagart VB. Therapeutic activity of enviroxime against rhinovirus infection in volunteers. Antimicrob Agents Chemother 1983; 23:671-675.

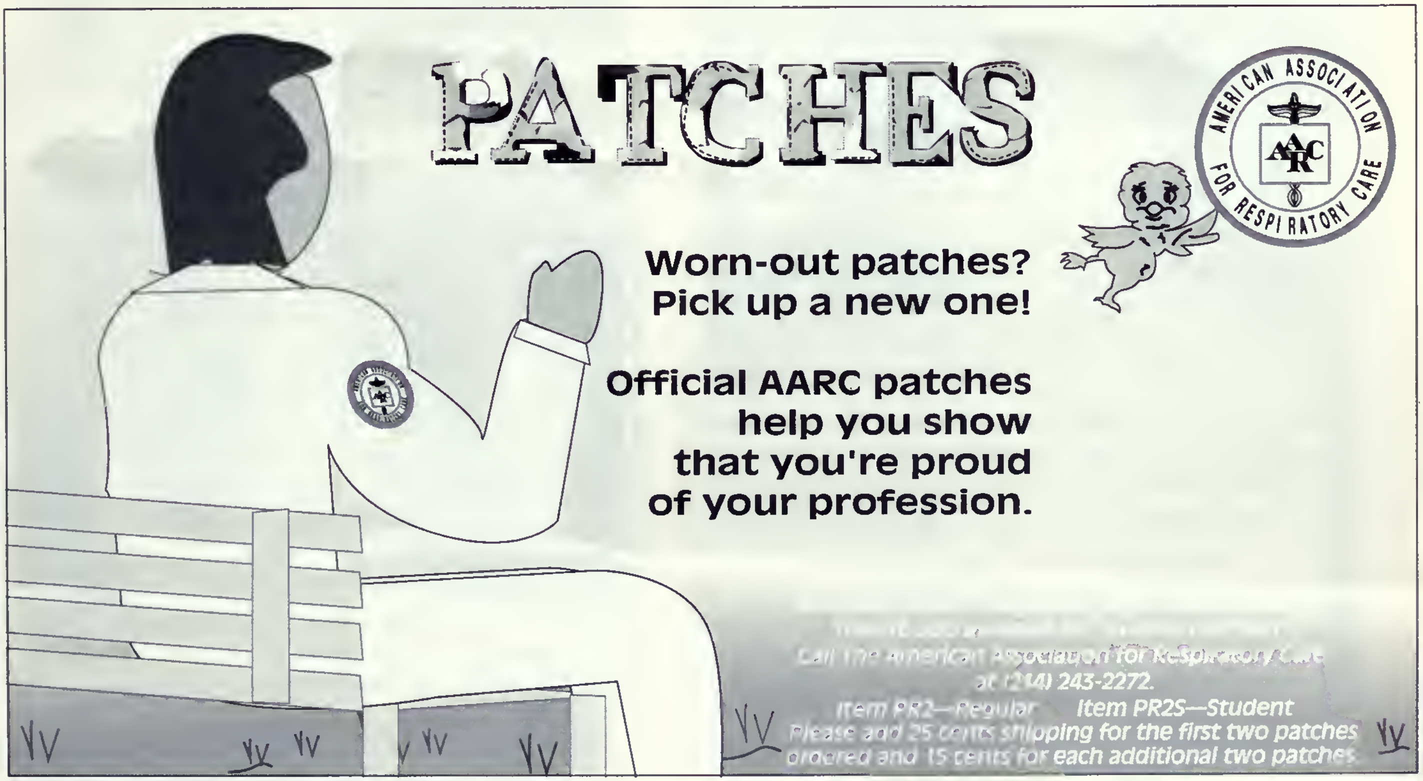
12. Tisdale M, Selway JWT. Effect of dichloroflavan (BW683c) on the stability and uncoating of rhinovirus type 1B. J Antimicrob Chemother 1984;14(Suppl A):97-105.
13. Phillpotts RJ, Wallace J, Tyrrell DAJ, Freestone D, Shepherd W. Failure of oral 4', 6-dichloroflavan to protect against rhinovirus infection in man. Arch Virol 1983;75:115-121.
14. Ishitsuka H, Ninomiya YT, Ohsawa C, Fuju M. Direct and specific inactivation of rhinovirus by chalcone RO 09-0410. Antimicrob Agents Chemother 1982;22:617-621.
15. Zerial A, Werner GH, Phillpotts RJ, Willman JS, Higgins PG, Tyrrell DAJ. Studies on 44 081 RP, a new antirhinovirus compound in cell cultures and in volunteers. Antimicrob Agents Chemother 1985; 27:846-850.
16. Smith TJ, Kremer MJ, Luo M, et al. The site of attachment in human rhinovirus-14 for antiviral agents that inhibit uncoating. Science 1986;223:1286-1293.
17. Tyrrell DAJ. Hot news on the common cold. Ann Rev Microbiol 1988;42:35-47.
18. Al-Nakib W, Tyrrell DAJ. A "new" generation of more potent synthetic antirhinovirus compounds: Comparison of their MICs and their synergistic interactions. Antiviral Res 1987;8:179-188.
19. Al-Nakib W, Higgins PG, Barrow GI, et al. Suppression of colds in human volunteers challenged with rhinovirus by a new synthetic drug (R 61837). Antimicrob Agents Chemother 1989;33:522-525.
20. Whitaker-Dowling P, Youngner JS. Antiviral effects of interferon in different virus-host cell systems. In: Pfeffer LM, ed. Mechanisms of interferon actions; Vol 1. Boca Raton FL: CRC Press, 1987:83-98.
21. Douglas RB, Moore BW, Miles HB, et al. Prophylactic efficacy of intranasal alpha$_2$ interferon against rhinovirus infections in the family setting. N Engl J Med 1986;314: 65-70.
22. McKinlay MA, Rossmann MG. Rational design of antiviral agents. Annu Rev Pharmacol Toxicol 1989;29:111-122.
23. Crumpacker CS. Molecular targets of antiviral therapy. N Engl J Med 1989;321:163-172.

JUST THE FAX. . .

Now it's easier than ever to place your recruitment classified word ad in the *AARC Times* RC Employment Opportunities Yellow Pages.

All you need to do is FAX your ad to Beth, and she'll take care of the rest.

JUST FAX TO (214) 484-2720


PATCHES
AMERICAN ASSOCIATION FOR RESPIRATORY CARE
AARC
Worn-out patches? Pick up a new one!
Official AARC patches help you show that you're proud of your profession.

[illegible]
Call the American Association for Respiratory Care at (214) 243-2272.
Item PR2—Regular Item PR2S—Student
Please add 25 cents shipping for the first two patches ordered and 15 cents for each additional two patches.

Charles G Durbin Jr MD and
Douglas B Eden BS RRT, Section Editors

Long-Term Coexistence of Interstitial Lung Disease and Pleural Effusion

KI Gourgoulianis MD, ST Gougoulakis MD, V Tsakraklides, and C Melissinos

A 50-year-old woman was admitted to our hospital because of shortness of breath. The woman was a nonsmoker. Ten years earlier, abnormalities had been noted on a chest radiograph (Fig. 1), but at that time the woman had no symptoms of respiratory disease. Eight years later, increased abnormalities were noted on a chest radiograph (Fig. 2).

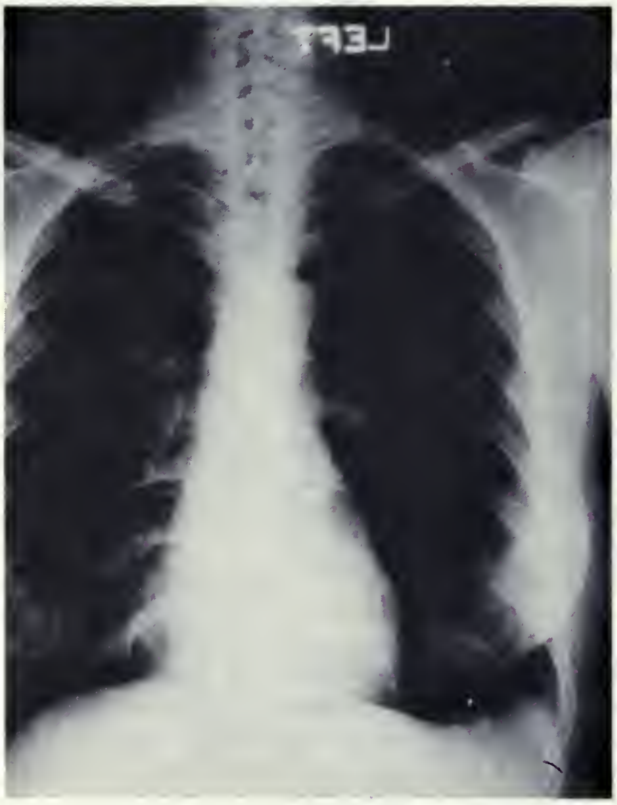


Fig. 1. Chest radiograph of a 40-year-old woman with no symptoms of respiratory disease, taken 10 years before she was admitted to the hospital for shortness of breath.

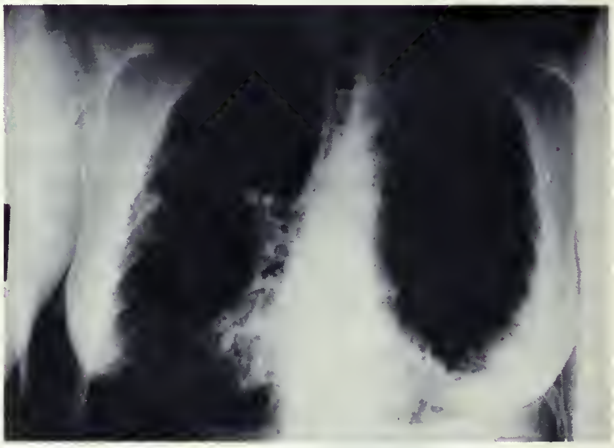


Fig. 2. Chest radiograph of the same woman (as in Fig. 1) at age 48 years, taken 2 years before she was admitted to the hospital for shortness of breath.

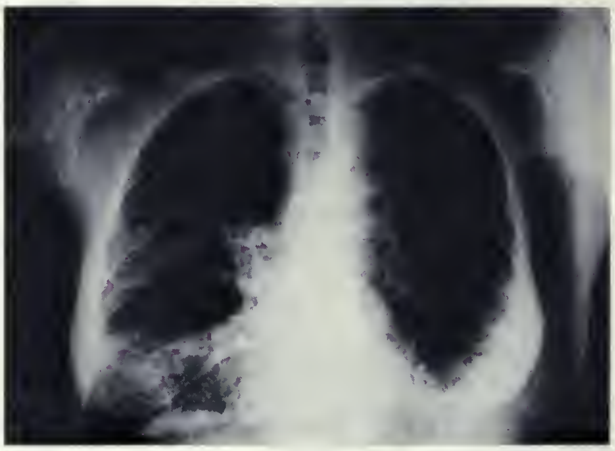


Fig. 3. Chest radiograph of the same woman (as in Figs. 1 & 2) at age 50 years, taken at the time of admission to the hospital for shortness of breath.

All of the authors are associated with the Pulmonary Diagnostic Department and Therapeutic Center "Hygeia," University of Athens, Athens, Greece.

On admission to our hospital, a chest radiograph was obtained (Fig. 3) and compared to the earlier radiographs. Chest auscultation revealed decreased intensity of breath sounds in the left lower zone and fine crepitations especially in the middle and lower zones. Analysis of arterial blood, while the patient breathed room air, revealed pH 7.47, P_{aCO_2} 32 torr [4.2 kPa], and P_{aO_2} 47 torr [6.3 kPa]. Pulmonary function testing revealed FVC 1.8 L (55% of predicted), FEV_1 1.6 L (64% of predicted), and FEV_1/FVC 88%.

Questions

Radiographic Findings: What abnormalities appear on the chest radiographs?

Possible Diagnoses: What pathologic processes could explain the clinical and radiologic course of this patient?

Diagnostic Confirmation: What further diagnostic tests are indicated?

Answers and Discussion on Next Page

How You Can Help Patients Stop Smoking

The National Heart, Lung, and Blood Institute has made available "How You Can Help Patients Stop Smoking: Opportunities for Respiratory Care Practitioners." This guide was developed in collaboration with the AARC and provides guidance on talking to patients about smoking. Plus, it tells you how to integrate a smoking intervention program into a respiratory care department. Includes strategies for community outreach and information on smoking intervention techniques and tools.

Single copies are free of charge by calling or writing:

The National Heart, Lung, and Blood Institute
Education Programs Information Center
4733 Bethesda Avenue,
Suite #530
Bethesda, MD 20814
(301) 951-3260

Yours free!

PUBLIC RELATIONS

BEGINS WITH YOU

Tell patients and their families that you belong to a unique group of health care professionals . . . identify yourself as a Respiratory Care Practitioner.

Practice good personal public relations every day — your efforts will make respiratory care a well-known, respected profession.

American Association for Respiratory Care
11030 Ables Lane • Dallas, TX 75229

Tell everyone you care by wearing *"Respiratory Care . . . Cares"* buttons.

Wear *"Respiratory Care . . . Cares"* buttons during visits to schools for health promotion activities, during health fairs, or on recruiting visits to respiratory care programs. After your presentation, distribute these colorful buttons, with a safety clasp, as mementos of your visit.
Item R6 — Pkg 50 - $13
(Member $6.50) plus shipping.

Call **(214) 243-2272** or FAX Your Order to **(214) 484-2720**

American Association
for Respiratory Care
11030 Ables Lane
Dallas, TX 75229-4593

Answers

Radiographic Findings: The chest radiograph taken 10 years prior to hospital admission (Fig. 1) shows a confluent shadow in the left lower zone. The radiograph taken 2 years prior to hospital admission (Fig. 2) reveals reticulonodular shadows in the middle and lower lung zones and left pleural effusion. The most recent radiograph (Fig. 3), taken on admission, reveals worsening of the abnormalities seen on the previous radiograph. All three chest radiographs were taken with the patient in an upright position.

Possible Diagnoses: Diseases that can result in long-term coexistence of interstitial lung disease and pleural effusion include systemic lupus erythematosus, rheumatoid arthritis, tuberculosis, bronchiolalveolar carcinoma, lymphoma, and leukemia.

Diagnostic Confirmation: Serologic tests and microbiologic and cytologic examination of sputum were negative. Bronchoscopy was not performed due to the presence of hypoxemia. Computed tomography of the chest showed, in addition to parenchymal abnormalities, enlargement of the mediastinal lymph nodes. Computed tomography of the abdomen showed enlargement of the spleen. An open-lung biopsy was performed. Histologic examination of specimens obtained from the lung parenchyma, pleura, and mediastinal lymph nodes revealed non-Hodgkin lymphoma characterized by small lymphocytes.

Discussion

Malignant lymphomas existing within the lung are rare. One large series of extranodal lymphoma, cited in Fraser and Paré,[1] showed that only in 3.6% of the cases was the respiratory system primarily affected. The patients are often asymptomatic, and the lung lesion is an incidental finding on a routine chest film. If symptoms are present, they usually include dyspnea, cough, chest pain, and weight loss.[2,3]

There are no universally accepted criteria for diagnosing a primary lymphoma of the lung. Pulmonary function tests are not specific. Radiographic findings are not diagnostic; however, large multiple shadows with pleural involvement are often consistent with lymphoma.[4,5] Open-lung biopsy can be performed safely and expeditiously and can yield an adequate sample of tissue from the diseased lung for examination. In a pulmonary lesion characterized by small lymphocytes, immunohistochemical studies are necessary to diagnose the disease process.[6]

The treatment of primary lymphoma of the lung includes chemotherapy, radiotherapy, and surgical removal of the lesion. In the case we report, prednisolone was administered 25 mg/day for 5 days and shortness of breath was alleviated. Surgical removal was ruled out because the lesion was not limited to the lung (nodules were also evident in the pleura and mediastinum). An alkylating agent, chlorambucil (Leuceran), was prescribed 5 mg bid. After 1 year of treatment with chlorambucil, our patient demonstrated radiographic and spirometric improvement: Pleural effusion was no longer evident, parenchymal shadows had lessened, FVC had increased to 2.15 L (66% of predicted), and FEV_1 had increased to 1.9 L (76% of predicted).

Little is known concerning the relative frequency and prognoses of histologic subtypes of primary lymphomas. The 2- and 5-year survival rates for lymphoma patients are 55% and 25%, respectively. When the lesions are completely removed, 75% of patients can be expected to survive more than 5 years.[4] In general, pulmonary lymphomas are said to carry a better prognosis than other lymphomas.[2]

REFERENCES

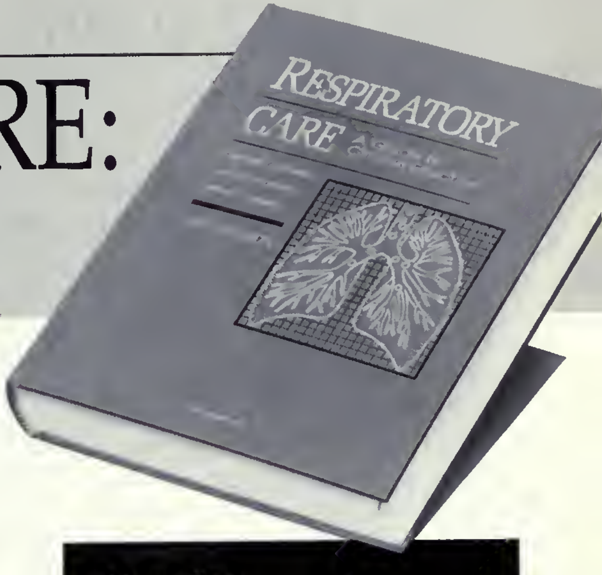
1. Fraser R, Paré P. Diagnosis of diseases of the chest. Philadelphia: WB Saunders, 1979.
2. Kennedy JL, Nathwani BN, Burke JS, Hill LR, Rappaport H. Pulmonary lymphomas and other pulmonary lymphoid lesions. Cancer 1985;56:539-552.
3. L'Hoste RJ, Filippa DA, Lieberman PH, Bretsky S. Primary pulmonary lymphomas. A clinicopathologic analysis of 36 cases. Cancer 1984;54:1397-1406.
4. Satzstein SL. Pulmonary malignant lymphomas and pseudolymphomas: Classification, therapy, prognosis. Cancer 1978;42:406-416.
5. Peterson H, Snider HL, Yam LT, Bowlds CF, Arnn EH, Li CY. Primary pulmonary lymphoma. A clinical and immunohistochemical study of six cases. Cancer 1985;56:805-813.
6. McCabe RE, Brooks RG, Catterall JR, Remington JS. Open lung biopsy in patients with non-Hodgkin's lymphoma and pulmonary infiltrates. Chest 1989;96:319-324.

Prepare your students *for practice on the front lines of respiratory care!*

RESPIRATORY CARE:

A GUIDE TO CLINICAL PRACTICE

THIRD EDITION



Edited by George G. Burton, M.D.; John E. Hodgkin, M.D., and Jeffrey J. Ward, M.Ed., RRT

62 Contributors

NEW Edition!

Recognized as the single most complete respiratory therapy resource...

Clinical in approach, *Respiratory Care* covers theory where appropriate, and technical aspects with precision and clarity. This book is divided into three sections for easy reference:

Section One: Respiratory Care Service and Education in the Modern Hospital

Covers the education of respiratory care workers, developing and staffing a department, current nursing practices in respiratory care, medicolegal aspects, and more.

Section Two: The Rational, Scientific Basis of Respiratory Therapy Techniques

Gives full descriptions of all tests, equipment, and modalities. Coverage ranges from pulmonary function testing to the process of ventilatory weaning.

Section Three: Respiratory Care in Critical Illnesses

Provides a step-by-step guide to respiratory care in specific critical illnesses.

...now even better in its new third edition!

The new third edition includes many new contributing authors, and is thoroughly updated to reflect current knowledge and technology. Seven new chapters cover:

- ✓ *Diagnosis and Therapy of Sleep-Disordered Breathing*
- ✓ *Hyperbaric Oxygen Therapy*
- ✓ *4th Generation Ventilation*
- ✓ *Home and Non-Traditional Site Respiratory Care*
- ✓ *Therapist-Peer Relationship*
- ✓ *Airway Management*
- ✓ *Fiberoptic Bronchoscopy*

1,056 Pages.
508 Illustrations. 239 Tables.
1991. (ISBN: 0-397-08909-X)
$65.00.

More fine respiratory care resources

Lynch and Deremee

Immunologically Mediated Pulmonary Diseases

Presents thorough coverage of immune mediated pulmonary diseases including all interstitial lung disorders. 560 Pages. 166 Illustrations. 38 Tables. 1991. (ISBN: 0-397-51051-9) $95.00.

Shelhamer et al / 68 Contributors

Respiratory Disease in the Immunosuppressed Host

Provides comprehensive and authoritative information on the epidemiology, incidence, diagnosis, and therapy of pulmonary disease in the immunosuppressed patient. 800 Pages. 221 Illustrations. 143 Tables. 1991. (ISBN: 0-397-51008-X) $100.00.

Problems in Respiratory Care

Clinically oriented articles address the problems encountered in daily practice. For both physicians and therapists. Published quarterly. $60.00 per year.

☎ *To order: call* ***TOLL FREE*** *(USA except AK)* ***1-800-638-3030 or Fax: 301-824-7390.*** *Or use the coupon below. Lippincott books are also available from your health science bookstore or Lippincott representative.*

Lippincott
A **Wolters Kluwer** Company

J. B. Lippincott Company • P.O. Box 1600, HAGERSTOWN MD 21741-1600

☐ **YES!** Please send me for 30 days' **on-approval** examination:

☐ **Burton 3/e** (ISBN: 0-397-08909-X) $65.00
☐ **Lynch** (ISBN: 0-397-51051-9) $95.00
☐ **Shelhamer** (ISBN: 0-397-51008-X) $100.00
☐ **Problems in Respiratory Care** $60.00 per year

Name ______________________
Address ______________________
City / State / Zip ______________________
Phone ______________________ Signature ______________________

☐ Payment enclosed* **(save postage & handling)**
☐ Bill me (plus postage & handling)
☐ Charge it:* **(save postage & handling)**
☐ MasterCard ☐ VISA
Card No. ______________ Exp. Date ______

***Add sales tax.** Prices in U.S. funds and subject to change. Orders subject to approval of Lippincott. Professional books may be tax deductible. Offer valid in U.S. and Canada only.

AM911324

4/91 RC

Circle 154 on reader service card

Books, Films, Tapes, & Software

Listings and Reviews of Books and Other Media

Note to publishers: Send review copies of books, films, tapes, and software to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229-4593.

Workbook To Accompany Respiratory Therapy Equipment, 4th ed, by Steven P McPherson RRT. Soft-cover, illustrated, 154 pages. St Louis: Mosby-Year Book Inc, 1991. $14.95.

This modestly priced laboratory practice manual for students should attract interest beyond the limited classroom setting. On occasion most of us are called upon to explain, demonstrate, or evaluate some mechanical property of the equipment we use. Simple, albeit practical, clues are contained in this little book that readily lend themselves to equipment evaluation in the field. Further, **Workbook** has a definite utilitarian value as a stand-alone publication.

Mr McPherson is an established authority on the medical devices used in respiratory care. His extensive experience in explaining the operational characteristics of these devices is apparent in this book.

The 15 chapters start logically with exercises in gas physics and end with a couple of exercises used to evaluate transport and home-care ventilators. The 52 exercises range in complexity from using a simple super syringe to evaluate the accuracy of a Wright Respirometer to comparing graphic waveforms of ventilator circuit problems induced in the laboratory. The book is richly illustrated with 51 crisp, attractive drawings and 44 graphs to be completed by the user.

The last half of the book (27 exercises) is devoted to mechanical ventilators. This is as it should be because of the depth and complexity of the subject matter. I was particularly impressed with Exercise 13-5, ''Subjective Comparison of Resistance to Flow through an Endotracheal Tube with and without Pressure Support.'' After completing this exercise by breathing through a 6.5-mm endotracheal tube, I had a dramatic appreciation for the use of pressure support to overcome system resistance and to reduce the work of breathing!

The home care practitioner should find a number of exercises to be relevant to that specialty area. McPherson has constructed exercises to test air compressors and oxygen concentrators as well as the home ventilators previously mentioned.

I did discover two inconsequential flaws that in no way detract from the substance of the book. Chapter 5, ''Artificial Airways,'' has no page number given in the table of contents—a proofreader error. Additionally, the author lists an endotracheal tube as being needed for Exercise 12-3, ''Evaluation of High Pressure Limit/Cycle on Rate and I:E with Bellows-Driven Ventilators.'' He then fails to explain how this tube is to be used. I could not ascertain its place in the exercise.

Without question, **Workbook To Accompany Respiratory Therapy Equipment** will be of greatest value and benefit to its target audience, respiratory therapy students. McPherson states in his preface that these largely self-directed ''exercises are designed in a straightforward manner so that the student can complete them easily and learn at the same time.'' I believe that he has accomplished his objective. Certainly, this 'student' profited from the manual.

Robert R Weilacher RRT
Director
Respiratory Care Service
Memorial Hospital
Palestine, Texas

Letters on topics of current interest or commenting on material in Respiratory Care will be considered for publication. The Editors may accept or decline a letter or edit it without changing the author's views. The content of letters as published may simply reflect the author's opinion or interpretation of information—not standard practice or the Journal's recommendation. Authors of criticized material will have the opportunity to reply in print. No anonymous letters can be published. Type letter double-spaced, mark it "For publication," and mail to Respiratory Care Journal, Box 29686, Dallas TX 75229.

Letters

Pulse Oximetry and Transcutaneous PO_2 Monitoring To Maintain Normoxia in Newborns

A recent article[1] and editorial[2] in Respiratory Care highlighted several issues concerning the use of pulse oximeters in the care of sick newborns. We were prompted to apply a similar analysis to data collected at our institution to determine our ability to utilize pulse oximeters (S_{pO_2}) and transcutaneous P_{O_2} (P_{tcO_2}) monitors to maintain normoxia in mechanically ventilated newborns. We reviewed the records of 25 newborns enrolled in a surfactant replacement therapy protocol (Exosurf, Burroughs Wellcome, Research Triangle Park NC) (gestational age = 31 ± 4 weeks, chronological age = 1.6 ± 0.7 days) for P_{aO_2} measurements and corresponding S_{pO_2} and P_{tcO_2} values recorded on respiratory care flowsheets. Arterial blood gas samples were obtained from indwelling intra-arterial catheters (P_{aO_2} ranged from 38 to 353 torr). Two different oximeters were used (Nellcor N-100, Nellcor Inc, Hayward CA, and Novametrix 505, Novametrix Medical Systems, Wallingford CT); unfortunately, we were not able to separate the data based on oximeter manufacturer. The Novametrix 850 (Novametrix Medical Systems, Wallingford CT) was used for all P_{tcO_2} measurements.

We found 226 simultaneously recorded observations of P_{aO_2}, P_{tcO_2}, and S_{pO_2} (mean samples per patient = 9 ± 5.4, range 8-22). We defined normoxia as a P_{aO_2} between 50 and 80 torr with an expected corresponding S_{pO_2} of 90-94% and P_{tcO_2} of 50-80 torr. Table 1 shows the sensitivity, specificity, and positive predictive value of the noninvasive monitors to maintain normoxic levels (P_{aO_2}). Our results indicate that there are differences in the reliability of the pulse oximeter and transcutaneous monitor in assisting the clinician to maintain normoxia. P_{tcO_2} 50-80 torr more accurately reflected normoxia than S_{pO_2} of 90-94% (sensitivity). However, the S_{pO_2} more reliably detected hypoxia and hyperoxia than did the P_{tcO_2} (specificity). Additionally, a P_{tcO_2} between 50 and 80 torr more frequently reflected a P_{aO_2} of 50-80 torr when compared to S_{pO_2} between 90-94% (positive predictive value). These results differ from those reported by Blanchette et al[1] and suggest alternative virtues of transcutaneous monitoring. However, the implications of these differences may be important. Our data were derived from clinically obtained recordings and reflect either methodologic inadequacy or the physiologic noise inherent in a routine clinical setting. The results reported by Blanchette et al[1] describe the outcome of carefully made prospective observations. These subtle but important differences and the mechanisms underlying these findings require future exploration to narrow the gaps between results obtained clinically and results obtained under more controlled circumstances.

Table 1. Comparison of Sensitivity, Specificity, and Positive Predictive Value of S_{pO_2} and P_{tcO_2} To Maintain P_{aO_2} between 50 and 80 torr

	S_{pO_2}	P_{tcO_2}
Sensitivity	0.21	0.80
Specificity	0.78	0.52
Positive Predictive Value	0.50	0.63

Frank Monaco RRT
Supervisor
Pediatric Pulmonary Diagnostic Center
Respiratory Care Services

Keith S Meredith MD
Staff Neonatalogist
Medical Director
Pediatric Respiratory Care

Memorial Hospital
Colorado Springs, Colorado

REFERENCES

1. Blanchette T, Dziodzio J, Harris K. Pulse oximetry and normoxemia in neonatal intensive care. Respir Care 1991;36:25-32.
2. Salyer J. Pulse oximetry in the neonatal intensive care unit (editorial). Respir Care 1991;36:17-20.

Blanchette and colleagues respond:

We commend Mr Monaco and Dr Meredith for investigating the accuracy of pulse oximetry and transcutaneous monitoring in their hospital's neonatal population. They acknowledge the use of two different pulse oximeters and used only one S_{pO_2} range in their comparative review. This approach could present a problem because differing bias for the Novametrix and Nellcor oximeters could presumably lead to different optimal S_{pO_2} limits for maintaining normoxemia. Nickerson et al found that the bias (mean of the differences between oximeter readings and the sum of oxy-, carboxy-, and methemoglobin) of the Nellcor N-100 was –0.44 and that of the Novametrix 500 was –1 over a range of S_{pO_2}s from 65-100%.[1] They noted that the bias changed (creating more of a discrepancy) as S_{pO_2} values decreased below 90%. In order to avoid these bias differences, we use Nellcor oximeters exclusively in our neonatal intensive care unit, allowing us to establish one appropriate S_{pO_2} range for normoxemia. We do not know how the 90-94% S_{pO_2} range was established for the purposes of the Monaco and Meredith chart review, but we doubt that one range would prove optimal for maintaining normoxemia with both the Nellcor and Novametrix oximeters.

Predictive value calculations, sensitivity, specificity, and positive predictive values can be confusing and require serious thinking to sort out. It appears fruitless to attempt to compare our results[2] to the results of Monaco and Meredith because of differing methodologies that include their use of two pulse oximeter brands, different S_{pO_2} and P_{O_2} limits, a more homogeneous patient population, the retrospective nature of the review, and the use of bidirectional limits for predictive value calculations as opposed to our two unidirectional predictive value calculations.

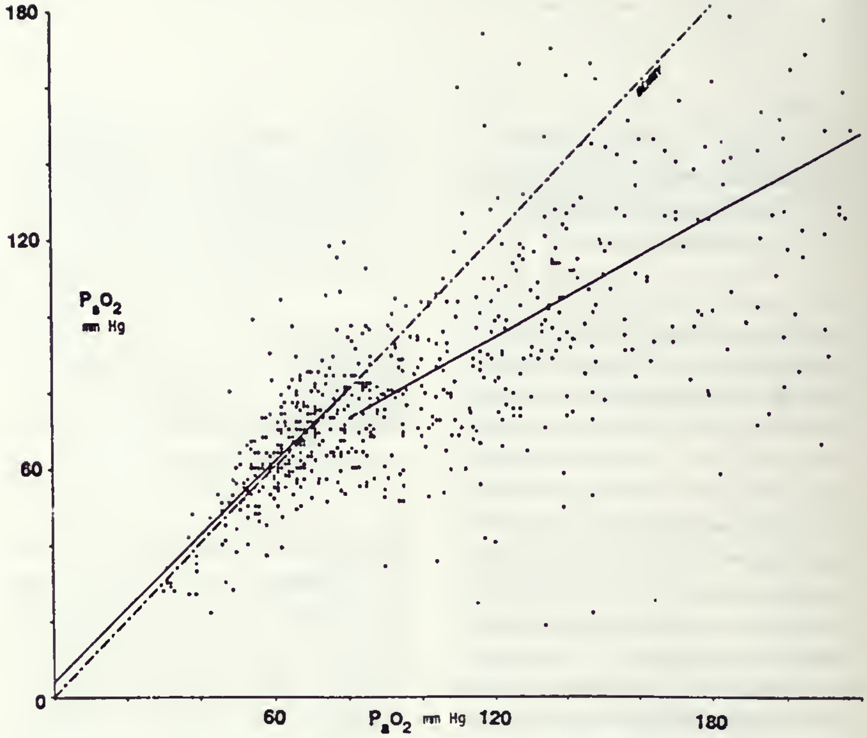


Fig. 1. The relationship of S_{pO_2} to P_{aO_2}, n = 723. Regression lines are shown for P_{aO_2} below and above 80 torr. (Adapted from Reference 3, with permission.)

Table 1. Advantages and Disadvantages of Pulse Oximetry over Transcutaneous P_{O_2} Monitoring

Advantages
Easy application
    no site preparation
Quick application
    no warm-up time
Faster response time
Easier maintenance
    no calibration necessary
    infrequent site changes
    no membrane changes
Safer skin application
    no heated sensor
    skin tears less likely
Wider range of applicability
    better accuracy in BPD
Accuracy evaluation
    pulse rate correlation
    waveform/pulse bar evaluation
Disadvantages
Motion artifact pronounced
Saturation vs P_{aO_2}

We agree that it is certainly important to evaluate the current place of transcutaneous monitoring in neonatal intensive care; and it is conceivable that transcutaneous P_{O_2} monitoring could be more accurate than pulse oximetry in assessing neonatal oxygenation. Although we did not report the data in our study,[2] we collected 152 P_{tcO_2} and and P_{tcCO_2} values from Transcend monitors (SensorMedics, Anaheim CA) while collecting our pulse oximetry data. We found the P_{tcO_2} numbers of limited value with a standard error of 13 from the 'actual' P_{aO_2} (ie, obtained by conventional analysis) and an increasing error as P_{aO_2} increased. These results are consistent with those reported (and shown in Fig. 1) by Palmisano and Severinghaus in a multicenter study of P_{tcCO_2} and P_{tcO_2} accuracy.[3] The comparative predictive value results from transcutaneous and pulse oximeter monitors is an interesting idea. We have seen no published studies using this approach, but many studies have demonstrated comparable accuracy for transcutaneous P_{O_2} and pulse oximeter monitors in acutely ill neonates by using other methods.[4-9] However, pulse oximetry has been demonstrated to be superior in bronchopulmonary dysplasia patients.[6-8] Although both monitoring techniques are relatively imprecise, there is increasing evidence that pulse oximetry is accurate and reliable in neonates.[2,4,10,11] Pulse oximetry's many practical advantages over transcutaneous monitoring (Table 1) understandably make it the oxygena-

FIRST PEEK AT OUR NEW LOW RANGE PEAK FLOW METER

Introducing ASSESS® Low Range for children and patients with limited or severely restricted expiratory flow rates

ASSESS Low Range offers the same standards of excellence as our ASSESS peak flow meter:

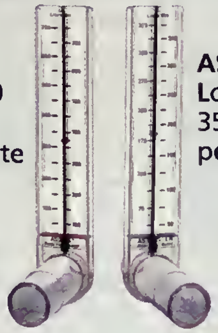
- Reproducible to ± 3 liters per minute*
- Proven accuracy† —highly correlated to ATS standards of spirometry*
- Easy to use
- Virtually indestructible
- Unconditional one-year warranty

* Meets *National Asthma Education Program Technical Requirements for Peak Flow Meters,* January, 1991.

†Shapiro S, Hendler J, Ogirala R, Aldrich T, Shapiro MB: An evaluation of the accuracy of Assess and Mini-Wright peak flow meters. *Chest 99*:358-362, 1991.

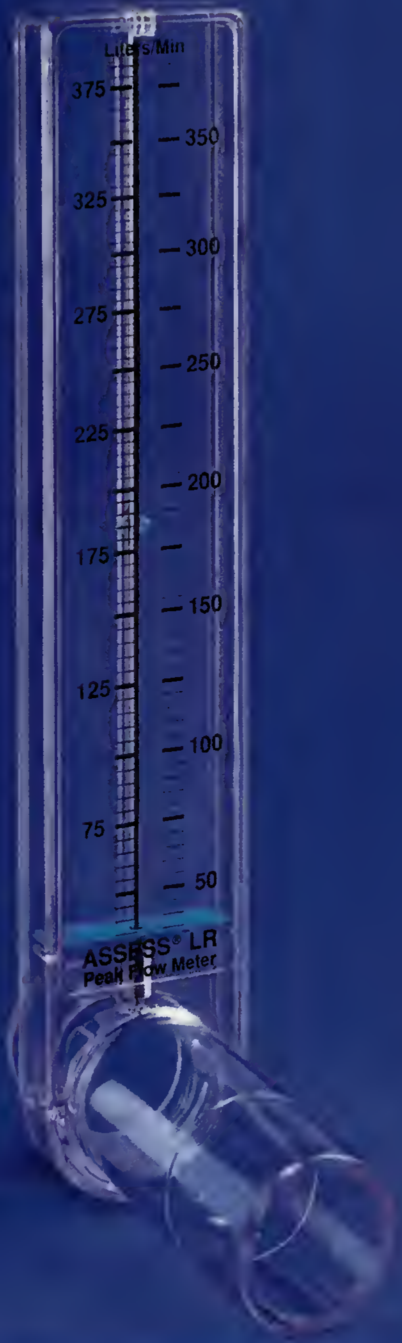
ASSESS® Peak Flow Meter

Setting the standard for peak flow monitoring



ASSESS
60 to 780
liters
per minute

ASSESS
Low Range
35 to 385 liters
per minute



HEALTHSCAN
Products Inc.

☐ Please send product information ☐ Please send an order form

☐ I prefer my patients to order directly. Send patient order forms.

NAME (please print)

HOSPITAL

ADDRESS

STATE ZIP PHONE

Mail to: **HealthScan Products Inc.,** 908 Pompton Avenue, Unit B-2, Cedar Grove, N.J. 07009-1292, or call toll free (800) 962-1266; in New Jersey, (201) 857-3414.

RC-4/91

Circle 109 on reader service card

tion monitor of choice in most neonatal intensive care units.[12]

Tim Blanchette MS RRT
Respiratory Therapist

John Dziodzio BA
Systems Analyst

Maine Medical Center
Portland, Maine

REFERENCES

1. Nickerson BG, Sarkisian C, Tremper K. Bias and precision of pulse oximeters and arterial oximeters. Chest 1988;93:515-517.
2. Blanchette T, Dziodzio J, Harris K. Pulse oximetry and normoxemia in neonatal intensive care. Respir Care 1991;36:25-32.
3. Palmisano BW, Severinghaus JW. Transcutaneous P_{CO_2} and P_{O_2}: A multicenter study of accuracy. J Clin Monit 1990;6:189-195.
4. Hay WW, Brockway JM, Eyzaguirre M. Neonatal pulse oximetry: Accuracy and reliability. Pediatrics 1989;83:717-722.
5. Wimberley PD, Helledie NR, Friis-Hansen B, et al. Pulse oximetry versus transcutaneous P_{O_2} in sick newborn infants. Scand J Clin Lab Invest 1987;47(Suppl 188):19-25.
6. Deckardt R, Steward DJ. Noninvasive arterial hemoglobin oxygen saturation versus transcutaneous oxygen tension monitoring in the preterm infant. Crit Care Med 1984;12:935-939.
7. Durand M, Ramanathan R. Pulse oximetry for continuous oxygen monitoring in sick newborn infants. J Pediatr 1986;109:1052-1056.
8. Ramanathan R, Durand M, Larrazabal C. Pulse oximetry in very low birth weight infants with acute and chronic lung disease. Pediatrics 1987;79:612-617.
9. Fanconi S, Doherty P, Edmunds JF, Barker GA, Bohn DJ. Pulse oximetry in pediatric intensive care: Comparison with measured saturations and transcutaneous oxygen tension. J Pediatr 1985;107:362-366.
10. Bucher HU, Fanconi S, Baeckert P, Duc G. Hyperoxemia in newborn infants: Detection by pulse oximetry. Pediatrics 1989;84:226-230.
11. Jennis MS, Peabody JL. Pulse oximetry: An alternative method for the assessment of oxygenation in newborn infants. Pediatrics 1987;79:524-528.
12. Salyer JW, Chatburn RL. Patterns of practice in neonatal and pediatric respiratory care. Respir Care 1990;35:879-888.

Directional-Tip Catheters: Are They 'Worth the Money'?

Directional-tip suction catheters are catheters manufactured with a bend or coude at the tip. The purpose of the directional tip is to allow selective suctioning of the main bronchi. It has been suggested that the inability to selectively suction the left bronchus may contribute to the higher incidence of complications of the left lower lobe.[1]

Determining the potential benefit to be derived from procedures performed and equipment purchased is an important facet of respiratory care department management. In trying to decide whether directional-tip suction catheters are 'worth the money,' I searched the literature for the answers to a series of questions and would like to share my findings.

How often will a directional-tip catheter enter the selected bronchus?

In adults, a straight-tip catheter introduced into the trachea most commonly enters the right-main bronchus because of the right bronchus's anatomic relationship to the trachea—It's a straight 'shot.' Anthony and Sieniwicz[2] and Kubota et al[3] have described the difficulties encountered during attempts to introduce straight-tip catheters employing several techniques to improve selected entry. Intentional entry into the left-main bronchus has been found to be most difficult.[2,4]

Kubota et al[3] found that preventing the directional-tip catheter from rotating as it is advanced through the endotracheal tube is the most important step for ensuring left-main bronchus entry. These investigators improved catheter design by adding a guide mark on the catheter enabling better control of rotation and thus better catheter placement. A subsequent study[1] of catheters utilizing a guide mark reported a 92% success rate for left-main bronchus entry. Directional-tip catheters with guide marks added are commercially available.

Will directional-tip suction-catheter use increase the effectiveness of pulmonary toilet?

My literature search produced no studies addressing this question; so, the answer appears to be unknown. However, we might postulate that selective suctioning of a main bronchus could be of benefit in a patient with a large mucus plug located specifically in a main bronchus.

Will atelectasis improve secondary to selected bronchus suctioning?

Bronchial obstruction is the most widely accepted cause of atelectasis. For many years, obstruction has been thought to be due to the presence of normal or infected secretions, bronchospasm, foreign materials, or congestion of bronchial walls.[5]

Marini et al[6] evaluated the use of fiberoptic bronchoscopy followed by "respiratory therapy" (ie, conventional suctioning, inhalation of aerosolized sympathomimetics, and chest percussion and postural drainage) compared to respiratory therapy alone, for treatment of acute lobar atelectasis. The bronchoscopist cannulated every segmental and most subsegmental bronchi and aspirated secretions until all visualized airways were clear. The investigators found no clinically important differences between respiratory therapy alone and with bronchoscopy for restoring lung-volume loss. It appears that placing a suction catheter a few centimeters into either main bronchus and suctioning is not likely to contribute to the resolution of atelectasis.

What is the cost of directional-tip catheters?

My informal survey of two manufacturers suggests that such catheters are a specialty item and, therefore, will cost a little more than conventional straight-tip catheters.

The efforts of clinicians and scientists to improve catheter design are to be applauded, and selective bronchus suctioning is now more possible than ever before. One can more readily gain access to the left-main bronchus with a directional-tip catheter equipped with guide mark. But, do they benefit the patient and are they worth the cost? I found nothing in the literature to indicate that improved pulmonary hygiene and better management of lobar atelectasis results from directional-tip catheter use. Prudent managers will consider the lack of evidence supporting the efficacy of use prior to purchase.

William R Anton RRT
Clinical Supervisor, Adult ICU
Respiratory Care Services
University of Washington
Medical Center
Seattle, Washington

REFERENCES

1. Kubota Y, Tatsuo M, Toyoda Y, et al. Selective bronchial suctioning in the adult using a curved-tipped catheter with a guide mark. Crit Care Med 1982;10:767-769.
2. Anthony JS, Sieniwicz DJ. Suctioning of the left bronchial tree in critically ill patients. Crit Care Med 1977;5:161-162.
3. Kubota Y, Mararibuchi T, Ohara M, et al. Evaluation of selective bronchial suctioning in the adult. Crit Care Med 1980;8:748-749.
4. Scott AA, Sandham G, Rebuck AS. Selective tracheobronchial aspiration. Thorax 1977;32:346-348.
5. Hamilton WK. Atelectasis, pneumothorax, and aspiration as postoperative complications. Anesthesiology 1961;22:708-721.
6. Marini JJ, Pierson DJ, Hudson LD. Acute lobar atelectasis: A prospective comparison of fiberoptic bronchoscopy and respiratory therapy. Am Rev Respir Dis 1979;119:971-977.

Letter Expressed Personal Viewpoint

Thank you for publishing my recent letter on PCIRV.[1] I would like to point out that my letter is based upon work done at Memorial Medical Center Inc in Savannah, Georgia, and The Medical College of Georgia in Augusta, Georgia. Although my present employer has an interest in my past publications, the recent letter in this Journal expresses my personal views. I had submitted this letter simply as a respiratory therapist living in Baltimore, Maryland, with an interest in PCIRV. My affiliation with Ohmeda is separate from my past research and personal views.

David C Lain PhD RRT RCP
Product Specialist
Ohmeda Respiratory Care
Columbia, Maryland

REFERENCES

1. Lain DC. Readers challenge pressure-controlled inverse-ratio ventilation editorial: And still more . . .. Respir Care 1991;36:124-128.

Start your own crusade with "Life and Breath"

"Life and Breath" can start you on your own crusade to educate the masses about respiratory care. This 6½-minute video vividly recreates the excitement and challenge of a career in respiratory care. It explains the roles of respiratory care practitioners in all settings, and discusses the educational requirements needed by therapists.

"Life and Breath" is an ideal student recruitment tool, and it can be used for so much more. Because this video provides an excellent overview of the profession, it can be presented to any group—from senior citizens, to students, to staff and other hospital professionals.

Send me ________ copy(ies) of *"Life and Breath"*

Item VT98V—VHS $40
(AARC members pay $35)
Please Add $3 Shipping For Each Tape

Bill to my P.O. No. ________
$ ________ enclosed.
Charge to my
☐ Visa ☐ MasterCard
Card No. ________
Expires ________
Signature ________
Name ________
Institution ________
Address ________
City ________
State ________ Zip ________
AARC Member No. ________

AARC, 11030 Ables Lane,
Dallas, TX 75229
3/89

SPECIAL MEMBER DISCOUNTS!

SAVE UP TO 10% OFF US SPRINT'S ALREADY LOW RATES

America's Best Long Distance Value, Even Better For Our Members.

Exciting news for your business bottom line! Your company can now enjoy the quality and price advantages of US Sprint® fiber optic long distance at special member discounts on out-of-state calls:

- 10% off daytime rates
- 4% off evening rates
- 3% off night and weekend rates
  OR:
- 5% off Dial 1 WATS daytime calls for customers with higher long distance usage

The best part is that these discounts are *in addition* to US Sprint's already low rates.

Fiber Optic Quality, 24-Hour Customer Service

US Sprint can offer us these extra savings because its nationwide 100% digital Fiber Optic Network not only sets a revolutionary new standard in sound quality but is the most cost-effective method of telephone transmission now in use. US Sprint can take you not only anywhere in the nation, but anywhere in the world you want to do business. You'll get 24-hour Operator Services, Directory Assistance and Customer Service. Plus you'll benefit from a full range of features that enhance your business productivity.

US Sprint FŌNCARDs℠ FREE For Our Members

FŌNCARD gives you US Sprint quality and savings away from your office. Every out-of-state call saves you 25¢* over AT&T's surcharge and up to 10%, 20%, even 30% over AT&T's standard rates. Your special discounts apply to all FŌNCARD charges, plus FŌNCARD is *free* with US Sprint long distance service.

*For calls greater than 11 miles in distance.

TO GET THIS EXCLUSIVE MEMBER BENEFIT,

CALL NOW TOLL-FREE 1 800 669-8585.

Notices

Notices of competitions, scholarships, fellowships, examination dates, new education programs, and the like will be listed here free of charge. Items for the Notices section must reach the Journal 60 days before the desired month of publication (January 1 for the March issue, February 1 for the April issue, etc). Include all pertinent information and mail notice to RESPIRATORY CARE Notices Dept, 11030 Ables Lane, Dallas TX 75229.

AARC SUMMER FORUM—July 12-14, 1991

Come and ''climb the highest mountain'' with your fellow therapists at the AARC Summer Forum in Vail, Colorado, at the Westin Hotel. Contact the AARC Conventions Dept. at (214) 243-2272.

AARC ANNUAL CONVENTION SITES & DATES

1991—Atlanta, Georgia, December 7-10
1992—San Antonio, Texas, December 12-15
1993—Nashville, Tennessee, December 11-14
1994—Las Vegas, Nevada, December 12-15
1995—Orlando, Florida, December 2-5

THE NATIONAL BOARD FOR RESPIRATORY CARE

1991 Examination and Fee Schedule

CRTT Examination

EXAMINATION DATE:	JULY 20, 1991
Applications Accepted Beginning:	March 1, 1991
Application Deadline:	May 1, 1991
EXAMINATION DATE:	NOVEMBER 9, 1991
Applications Accepted Beginning:	July 1, 1991
Application Deadline:	September 1, 1991

CPFT Examination

EXAMINATION DATE:	JUNE 1, 1991
Applications Accepted Beginning:	December 1, 1990
Application Deadline:	April 1, 1991

RRT Examination

EXAMINATION DATE:	JUNE 1, 1991
Applications Accepted Beginning:	December 1, 1990
Application Deadline:	February 1, 1991
EXAMINATION DATE:	DECEMBER 7, 1991
Applications Accepted Beginning:	June 1, 1991
Application Deadline:	August 1, 1991

RPFT Examination

EXAMINATION DATE:	DECEMBER 7, 1991
Applications Accepted Beginning:	July 1, 1991
Application Deadline:	September 1, 1991

Fee Schedule

Entry Level CRTT—new applicant:	$ 75.00
Entry Level CRTT—reapplicant:	$ 50.00
RRT Written and Clinical Simulation—new applicant:	$175.00
Written Registry Only new applicant:	$ 75.00
Written Registry Only reapplicant:	$ 50.00
Clinical Simulation Only new and reapplicant:	$100.00
Entry Level CPFT—new applicant:	$100.00
Entry Level CPFT—reapplicant:	$ 80.00
Advanced RPFT—new applicant:	$150.00
Advanced RPFT—reapplicant:	$130.00
CRTT Recredentialing:	$ 25.00
RRT Recredentialing:	
Written Registry Examination	$ 25.00
Clinical Simulation Examination	$ 65.00
CPFT Recredentialing:	$ 25.00
RPFT Recredentialing:	$ 90.00
Membership Renewal CRTT/RRT/CPFT/RPFT	$ 12.00

8310 Nieman Road • Lenexa, Kansas 66215 • (913) 599-4200

Calendar of Events

Not-for profit organizations are offered a free advertisement of up to eight lines to appear, on a space available basis, in Calendar of Events in Respiratory Care. Ads for other meetings are priced at $5.50 per line and require an insertion order. Deadline is the 20th of month two months preceding the month you wish the ad to run. Submit copy and insertion orders to: Calendar of Events, Respiratory Care, 11030 Ables Lane, Dallas TX 75229.

AARC & AFFILIATES

May 1-3 in Rapid City, South Dakota. Rapid City Regional Hospital hosts the annual convention of the SDSRC. Featured speakers (including WJ O'Donohue Jr MD, Robert Kacmarek PhD RRT, and Anthony Talbert MD) discuss neonatal, pediatric, and adult critical care issues. Contact Terry Anderson RRT, Respiratory Care Department, 1-800-232-9287.

May 2-3 in Bangor, Maine. The Maine Society for Respiratory Care presents its Spring Seminar '91 and sputum bowl competition at the Bangor Ramada Inn. Contact Janie Barthelette at (207) 596-8485.

May 7-9 in LaCrosse, Wisconsin. The WSRC presents its 21st annual convention at the LaCrosse Convention Center/Radisson Hotel. This entertaining and educational meeting features such noted speakers as Patrick Dunne MEd RRT — President, AARC; Neil MacIntyre MD and David Pierson MD discussing pediatric, adult, and management topics. Contact Tami Meier RRT, (608) 263-7050, or Laura Taylor RRT, (608) 785-0530.

May 10 in Industry Hills, California. CSRC, Chapter IV, & Kaiser Permanente present Pediatric Pulmonary Care at Sheraton Hotel and Resort. The meeting features CV/HFV in PICU and cardiac surgery topic and a poster session. CSRC Scholarship Golf Tournament, top 25 rated courses in the U.S., May 11. Contact Dennis Vinson (213) 667-5176.

May 16-17 in Wichita, Kansas. The KRSC presents its 14th Annual Education Seminar at the Airport Hilton. Topics range from future directions of the profession to PFT, asthma, and critical care issues. Scheduling allows for golf, exhibits and a great time for everyone. Contact Don Richards MS RRT, VA Medical Center,(316) 685-2221.

May 28-31 in Jekyll Island, Georgia. The Georgia/South Carolina Region VI presents its 15th Annual Conference and Assembly at the Holiday Inn, Jekyll Island. Contact Mike Payne RRT, 730 South Pleasantburg Dr, Suite 525, Greenville SC 29607. (803) 879-0130.

May 29-31 in Brainerd, Minnesota. The MSRC invites all practitioners to its spring educational meeting. An excellent educational program is featuredin the enjoyable setting of Madden's Resort in Northern Minnesota. Contact Gary Johnson, North Country Regional Hospital, 1100 West 38th St, Bemidji MN 56601, (218) 751-5430 (7 AM—9:30 PM CST).

June 12-14 in Vail, Colorado. The CSRC State Convention's theme "Bringing It All Together" focuses on the crossover between hospital and home care. A golf tournament is featured for the morning of the 12th, followed by a barbecue picnic in the that evening. Contact Jim Bowman, Vencor Hosn, 1920 High St, Denver CO 80218, (303) 320-5871.

June 12-14 in St Charles, Illinois. The ISRC presents its annual convention, "It's a Jungle Out There," to be held at Pheasant Run. Contact Trudy Watson RRT, Black Hawk College, 6600 34th Avenue, Moline IL 61265. (309) 796-1311, ext. 3303 or Vince Madama RRT, Rock Valley College, 3301 N Mulford Drive, Rockford IL 61103. (815) 654-4413 or (815) 654-4410.

June 27-29 in Monterey, California. The CSRC holds its 23rd annual meeting at the Doubletree Inn and Monterey Convention Center. Conference topics include "Liquid Perfluorchemical Ventilation," "DNAse Aerosol Therapy in Cystic Fibrosis," "Adult Exosurf" and Professor's Rounds, a 4-hour presentation featuring Neil MacIntyre MD, David Pierson MD, John Marini MD, and Robert Kacmarek PHD RRT. Contact John Bigler, Executive Director, CSRC, 24307 Magic Mountain Parkway #288, Valencia Ca 91355. To register call (800)-543-CSRC (2772).

OTHER MEETINGS

May 4-7 in Atlanta, Georgia. The Department of Cardiopulmonary Care Sciences at Georgia State University presents the seminannual registry review program. The program is designed to prepare candidates for the written and the clinical simulation examinations. Contact Vijay Deshpande, Assistant Professor, Dept of Cardiopulmonary Care Sciences, Georgia State University, Atlanta GA 30303. (404) 651-3037.

May 12-15 in Anaheim, California. The American Lung Association and the American Thoracic Society host an International Conference in Anaheim. Contact Maureen J O'Donnell, Associate Director, Professional Development, American Lung Association, 1740 Broadway, New York NY 10019-4374.

May 17-18 in Las Vegas, Nevada. The American Lung Association of Nevada sponsors the 6th Annual Southern Nevada Respiratory Health Conference at the Sahara Hotel. Contact American Lung Association of Nevada, PO Box 44137, Las Vegas NV 89116. (702) 454-2500.

August 25-September 1, Caribbean Cruise. Cruise the Western Caribbean aboard the SS Sea Breeze while earning 8 CRCE credits. Topic is "Aid for AIDS." $895 prepaid includes airfare, cruise, transfers, food, and entertainment. Friends and family welcome. Call or write Dream Cruises, 10882 LaDona Ave, Garden Grove CA 92640. 1-800-462-3628.

1991 Call for Abstracts

The American Association for Respiratory Care and its science journal, RESPIRATORY CARE, invite submission of brief abstracts related to any aspect of cardiorespiratory care. The abstracts will be reviewed, and selected authors will be invited to present papers at the Open Forum during the AARC Annual Meeting in Atlanta, Georgia, December 7-10, 1991. Accepted abstracts will be published in the November 1991 issue of RESPIRATORY CARE. Membership in the AARC is not necessary for participation.

Specifications

An abstract may report (1) an **original study**, (2) the **evaluation of a method or device**, or (3) a **case or case series**. Topics may be aspects of adult acute care, continuing care/rehabilitation, perinatology/pediatrics, cardiopulmonary technology, health occupations education, or management of personnel and health-care delivery. The abstract may have been presented previously at a local or regional—but not national—meeting and should not have been published previously in a national journal.

The abstract will be the only evidence by which the reviewers will decide whether the author should be invited to present a paper at the Open Forum. Therefore, *the abstract must provide all important data, findings, and conclusions.* Give specific information. Do not write such general statements as "Results will be presented" or "Significance will be discussed."

Essential Content Elements

An **original study** abstract ***must*** include (1) Introduction: statement of research problem, question, or hypothesis; (2) Method: description of research design and conduct in sufficient detail to permit judgment of validity; (3) Results: statement of research findings with quantitative data and statistical analysis; (4) Conclusions: interpretation of the meaning of the results.

A **method/device evaluation** abstract ***must*** include (1) Introduction: identification of the method or device and its intended function; (2) Method: description of the evaluation in sufficient detail to permit judgment of its objectivity and validity; (3) Results: findings of the evaluation; (4) Experience: summary of the author's practical experience ***or*** a notation of lack of experience; (5) Conclusions: interpretation of the evaluation and experience. Cost comparisons should be included where possible and appropriate.

A **case report** abstract ***must*** report a case that is uncommon or of exceptional teaching/learning value and must include: (1) case summary and (2) significance of case. Content should reflect results of literature review. The author(s) should have been actively involved in the case and a case-managing physician must be a co-author or must approve the report.

Abstract Format and Typing Instructions

An optical scanner will be used to process abstracts. First line of abstract should be the title. Title should explain content. Type or electronically print the abstract ***double-spaced*** on ***plain white bond paper***, on ***one page*** only (copier bond is excellent). Do not underline or boldface and insert only one letter space between sentences. Provide a 1-inch margin top and bottom, a ½-inch left margin, and an approximate ½-inch ragged-right margin. Text may be submitted on diskette but must be accompanied by a hard copy.

No identification of authors or institutions is to appear on the abstract sheet or in the abstract itself. Make the abstract all one paragraph. Data may be submitted in table form ***provided the table width is limited to 60 letter spaces*** (ie, letters or numbers plus necessary blank spaces = 60). ***No*** figures or illustrations are to be attached to the abstract.

Type all information required to complete the author information form on the other side of this page. A photocopy of good quality may be used.

Standard abbreviations may be employed without explanation. A new or infrequently used abbreviation should be preceded by the spelled-out term the first time it is used. Any recurring phrase or expression may be abbreviated if it is first explained.

Check the abstract for (1) errors in spelling, grammar, facts and figures; (2) clarity of language; (3) conformance to these specifications. An abstract not prepared as requested may not be reviewed.

Questions about abstract preparation may be telephoned to the editorial staff of RESPIRATORY CARE at (214) 243-2272.

Deadlines

The mandatory Final Deadline is June 5 (postmark). Authors will be notified of acceptance or rejection ***by letter only***—to be mailed by August 15.

Authors may choose to submit abstracts early. Abstracts received by March 20 will be reviewed and the authors notified by April 26. Rejected abstracts will be accompanied by a written critique that should in many cases enable authors to revise their abstracts and resubmit them by the final deadline (June 5).

Mailing Instructions

Mail (Do not fax!) 1 copy of the abstract, 1 author information sheet, and a stamped, self-addressed postcard (for notice of receipt) to:

RESPIRATORY CARE
11030 Ables Lane
Dallas TX 75229

1991 OPEN FORUM
AUTHOR INFORMATION SHEET

Please type:

Abstract title

Principal author	Institution

Corresponding author	Presenter
Mail station, building, or room	Mail station, building, or room
Institution	Institution
Street address	Street address
City, State, Zip	City, State, Zip
Telephone	Telephone

Co-author	Institution
Co-author	Institution
Co-author	Institution

Mail, with abstract and stamped self-addressed postcard, to Respiratory Care Open Forum
11030 Ables Lane, Dallas TX 75229

RESPIRATORY CARE

Instructions for Authors and Typists

These Instructions are meant to guide authors and typists, including veterans in those roles, in the production of quality manuscripts. Perfection is not expected, but the well-prepared manuscript has the best chance for prompt review and early publication.

General Requirements

Submissions should (1) be related to respiratory care, (2) be planned for one of the publication categories below, and (3) be prepared as indicated in these Instructions. A letter accompanying the manuscript must specify the intended publication category, be signed by all the authors, and, when there are two or more authors, state that "We, the undersigned, have all participated in the work reported, read the accompanying manuscript, and approved its submission for publication."

Publication Categories

Research Article (Study): A report of an original investigation.

Evaluation of a Device/Method/Technique: A description and evaluation of an old or new device, method, technique, or modification.

Case Report: A report of a clinical case that is uncommon or of exceptional teaching value. The author(s) must have been associated with the case. A case-managing physician must be one of the authors or, if not an author, must supply a letter approving the manuscript.

Case Series: Like a Case Report but including a number of cases.

Review Article: A comprehensive, critical review of the literature and state of the art of a pertinent topic that has been the subject of 40 or more published research papers.

Overview: A critical review of a pertinent topic about which not enough research has been published to merit a Review Article.

Update: A report of subsequent developments in a topic that has been critically reviewed (not necessarily in this journal).

Point of View: A paper expressing the author's personal opinions on a pertinent topic.

Special Article: If a paper does not fit one of the foregoing categories but is pertinent, the editors may consider it as a Special Article.

Editorial: A paper that draws attention to a pertinent concern.

Letter: A signed communication about material published in this journal or on topics of interest or value to readers.

Blood Gas Corner: A brief, instructive case report (real or fictional) involving invasively or noninvasively obtained respiratory care blood data, followed by questions for readers—with answers and discussion.

PFT Corner: Like Blood Gas Corner but involving pulmonary function testing.

Test Your Radiologic Skill: Like Blood Gas Corner and PFT Corner but involving pulmonary-medicine radiography and including one or two 4 × 5 or 5 × 7 inch prints of radiographs. The case must be real.

Review of Book, Film, Tape, or Software: Anyone interested in writing a review can discuss it with an editor.

Editorial Consultation and
Author's & Typist's Kit

To discuss a writing project, write to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229 or call 214/243-2272.

Authors are urged to obtain the RESPIRATORY CARE Author's & Typist's Kit. The Kit provides *authors* with specific guidance about writing a research paper, writing a case report, converting to and from SI units, and in-house manuscript review. *Typists* can use the Kit's Model Manuscript, a list of journal name abbreviations, and a copy of these Instructions. The Kit is free from the Journal office.

Preparing the Manuscript

General Concerns—*Typist*

- Double-space ALL lines, including those in references, figure legends, and tables. Do not justify right margins.
- Number pages in upper right corner and leave margins of 1½" or more on all four sides of the page.
- For research articles, follow format of Model Manuscript, Respir Care 1984;29:182 (Feb 1984).
- Meticulously follow instructions for typing references.

General Concerns—*Author:*

- Structure manuscript as specified hereafter.
- Provide all requested information on title page as specified hereafter.
- Proofread manuscript for completeness, clarity, grammar, spelling; be sure all references, figures, and tables are cited in the text.
- Consider having paper reviewed in-house before submission.
- Have all co-authors proofread and approve manuscript and sign submission letter.

Manuscript Structure

Most kinds of papers have standard parts in a standard order. However, papers can vary individually, and not every paper will have all the parts listed here.

Research Article: Title page, abstract page, continuous text (Introduction, Materials & Methods, Results, Discussion), Product Sources page, Acknowledgments page, references, tables, figure legends. Please consult "Writing a Research Paper," Respir Care 1985;30:1057 (Dec 1985) and Model Manuscript, Respir Care 1984;29:182 (Feb 1984).

Evaluation of Device/Method/Technique: Title page, abstract page, continuous text (Introduction, Description of Device/Method/Technique, Methods of Evaluation, Results of Evaluation, Discussion), Product Sources page, Acknowledgments page, references, tables, figure legends.

Case Report or Case Series: Title page, abstract page, continuous text (Introduction, Case Summary, Discussion), Acknowledgments page, references, tables, figure legends. Also see "How To Write a Better Case Report," Respir Care 1982;27:29 (Jan 1982).

Review Article: Title page, Table of Contents page, continuous text (Introduction, History, Review of Literature, State of the Art, Discussion, Summary), references. May include figures & tables. No abstract. Table of Contents optional. Other formats may be appropriate.

Overview, Update, Point of View, or Special Article: Title page, text (introduction, message), references, tables, figure legends. No abstract.

Letter: Title page (provide a title), text, writer's name & affiliation, references. Tables & figures may be included. Double-space everything. Write "For Publication" on title page.

Structure: Important Details

Title Page: List title of paper, all authors' full names, degrees, credential letters, professional positions, and affiliations. List correspondence address, telephone number, and reprint address if desired. Name sources of grants or other support. Identify any author's consulting or commercial relationships that pertain to the paper's topic.

Abstract Page: Number this Page 1. List paper's title but omit authors' names. Abstract should be 200 words or less and must be informative, briefly specifying main points of paper, such as methods, results, and conclusions drawn.

Statistical Analysis: In research articles, identify statistical tests and chosen level of significance in the Methods section. In Results section, report actual P values.

Figures (illustrations): All photographs, diagrams, & graphs must be numbered as Figure 1, Figure 2, etc, according to the order in which each is first mentioned in the text. Photographs must be glossy prints 5 × 7 to 8 × 10 inches and should be black & white unless color is essential. Letters and numerals must be neat and large enough to remain legible if figure is reduced in size for publication. Final figures must be of professional quality, but 'rough' sketches may accompany the submitted manuscript, with final figures to be prepared after review. Identify each figure on back with a stick-on label showing figure number and arrow indicating top; omit author's name. Cover label with clear tape so ink will not smudge other prints. Supply three sets of unmounted figures. If figure has been published before, include copyright-holder's written permission to use it.

Figure Legends: List figure legends on a separate page, not on figures. If a figure has been published before, list the source in the legend.

Tables: Type each table on a separate page. Avoid more than 8 columns across. Continue a deep table on following pages. Give each table a number and descriptive title, placed above the table. Double-space ALL lines in tables, including column headings and footnotes.

Drugs: Brand names may be given, but always also show generic names.

Units of Measurement: In addition to conventional units of measure, show SI values and units in brackets after conventional expressions: ie, "PEEP, 10 cm H_2O [0.981 kPa]." For conversion to SI, see RESPIRATORY CARE 1988;33:861-873 (Oct 1988).

Commercial Products: If three or fewer commercial products are named in the text, list the manufacturer's name and location in parentheses the first time each is mentioned. If four or more products are named, do not list manufacturers in the text; instead, name the products and manufacturers in a Products Sources list at the end of the text. Provide model numbers when available.

Abbreviations: Use an abbreviation only if the term occurs several times in the paper. Write out the full term the first time it appears, followed by the abbreviation in parentheses. Thereafter, employ the abbreviation alone. Never use an abbreviation without defining it. Do not create new abbreviations unless absolutely necessary.

References:

- Use references to support statements of fact, indicate sources of information, or guide readers to further pertinent literature.
- Cite only published works—or works accepted for publication. When listing an accepted but still unpublished work, designate the accepting journal's name, followed by "(in press)."
- In the text, cite references by superscript numerals (half space above text), not in parentheses. The first reference cited in the text is number 1, the next is number 2, etc.
- In the reference list, place the cited works in numerical order.
- For the reference list, obtain author names, article and book titles, dates, volume and page numbers from the *original* cited articles and books, not from secondary sources such as other articles' reference lists, which often are inaccurate.
- Type references in medical-journal style. Examples appear at the end of these Instructions. Abbreviate journal names as in *Index Medicus.* A list of many journal-name abbreviations was published in Respir Care 1988;33:1050 (Nov 1988).
- DOUBLE-SPACE the lines of references.
- List ALL authors' names. Do not use "et al" to substitute for names.
- Identify abstracts, editorials, and letters as such. See examples.

Personal Communications, Unpublished Papers, and Unpublished Observations: List unpublished items in parentheses in the text, not in the reference list.

Examples of How To Type References

Notes: Although the examples here are printed with single-spaced lines, please double-space references in manuscripts. Also, note that words in article and book titles are not capitalized—except proper names.

Standard Journal Article:

1. Shepherd KE, Johnson DC. Bronchodilator testing: An analysis of paradoxical responses. Respir Care 1988;33:667-671.

Corporate Author Journal Article:

2. American Association for Respiratory Care. Criteria for establishing units for chronic ventilator-dependent patients in hospitals. Respir Care 1988;33:1044-1046.

Article in Journal Supplement:

(Journals differ in their methods of numbering and identifying supplements. Supply sufficient information to allow retrieval.)

3. Reynolds HY. Idiopathic interstitial pulmonary fibrosis. Chest 1986;89(3, suppl):139s-143s.

Abstract in Journal:

(Abstracts are not strong references; when possible, full papers should be cited. When cited, abstracts should be identified as such.)

4. Lippard DL, Myers TF, Kahn SE. Accuracy of pulse oximetry in severely hypoxic infants (abstract). Respir Care 1988;33:886.

Editorial in Journal:

5. Rochester DF. Does respiratory muscle rest relieve fatigue or incipent fatigue? (editorial). Am Rev Respir Dis 1988;138:516-517.

Letter in Journal:

6. Smith DE, Herd D, Gazzard BG. Reversible bronchoconstriction with nebulised pentamidine (letter). Lancet 1988;2:905.

Personal Author Book:

7. Nunn JF. Applied respiratory physiology. New York: Appleton-Century-Crofts, 1969.

Note: To specify pages cited in a book, place a colon after the year and then list the page(s). Examples: 1969:85 (one page), 1963:85-95 (series of contiguous pages), 1963:85,95 (separated pages).

Corporate Author Book:

8. American Medical Association Department of Drugs. AMA drug evaluations, 3rd ed. Littleton CO: Publishing Sciences Group, 1977.

Book with Editor, Compiler, or Chairman as 'Author':

9. Guenter CA, Welch MH, eds. Pulmonary medicine. Philadelphia: JB Lippincott, 1977.

Chapter in Book:

10. Pierce AK. Acute respiratory failure. In: Guenter CA, Welch MH, eds. Pulmonary medicine. Philadelphia: JB Lippincott, 1977:171-223.

Submitting the Manuscript

After preparing the manuscript according to these Instructions, perform a final proofreading and check for accuracy and completeness. Then mail three copies of the manuscript and three sets of figures to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229 (or Federal Express to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229). Manuscript copy on IBM-compatible or Macintosh disks in addition to the requisite three hard copies will facilitate processing (Macintosh preferred). Enclose a letter as specified under **General Requirements** at the beginning of these Instructions. Do not submit material that has been published or is being considered elsewhere.

Author's Checklist

1. Is paper for a listed publication category?
2. Does cover letter meet specifications?
3. Is title page complete?
4. Are all pages double-spaced and numbered?
5. Are all references, figures, and tables cited in the text?
6. Are references typed in requested style?
7. Have SI values been provided?
8. Has all arithmetic been checked?
9. Has manuscript been proofread by all authors?

News releases about new products and services will be considered for publication in this section. There is no charge for these listings. Send descriptive release and glossy black and white photographs to RESPIRATORY CARE Journal, New Products and Services Dept, 11030 Ables Lane, Dallas TX 75229.

New Products & Services

O$_2$ CONCENTRATION MONITOR. The Oxygen Threshold Monitor (OTM) is designed to provide the oxygen-dependent patient with increased peace of mind by featuring a color-coded meter that warns the patient when oxygen concentration from a concentrator falls below a minimum threshold. According to the manufacturer, the OTM can be easily installed into or on the exterior of virtually any oxygen concentrator in minutes and is capable of measuring oxygen concentration in the range of 50 to 99%, with an accuracy of ± 5%. Ceramatec Inc, Cerion Division, Dept RC, 2425 South 900 West, Salt Lake City UT 84119. (801) 972-2455.

COMBINATION SPIROMETRY/ECG SYSTEM. According to the manufacturer, the lightweight, compact Cardiovit CS-6/12Z unit has the ability to acquire 10 seconds of simultaneous 12-lead information and to produce an 8.5 × 11-inch chart-ready printout of the resting ECG. A large liquid crystal display provides preview of real-time ECG and user prompts for custom report formatting, and the ECG can be printed in 3 or 6 channels. The optional Spirovit SP-100 spirometry feature permits pulmonary function testing, which, according to the manufacturer, meets ATS standards for full reimbursement. The SP-100's pneumotach is designed to enable fast and easy sterilization. Schiller, Dept RC, 15461 Red Hill Ave, Suite E, Tustin CA 92680. (800) 247-8775.

PORTABLE METABOLIC COMPUTER. The Oxymax-H is a portable metabolic measurement system consisting of two parts: a metabolic computer with O$_2$ and CO$_2$ analyzers and a precisely controlled air supply and a laptop PC/AT-compatible computer. According to the manufacturer, the instrument, which measures 9″ × 17″ × 51″ (23 × 43 × 51 cm) and weighs 45 lb (21 kg), can be easily transported to patients confined to their homes. The metabolic data are stored on an internal hard disk and can be transferred to another computer by way of floppy disks or communications facilities. Data can also be printed in either tabular or graphic formats, using an attached printer. During measurement, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, respiratory exchange ratio, and caloric expenditure are plotted in real time on the screen. Because the system operates on the open-flow indirect calorimetry principle, masks, canopies, or tents can be used for the collection of expired gases. Due to a large range of available air flows, the system can be used in pediatric and adult patients, and for sports-medicine purposes. Columbus Instruments, Dept RC, PO Box 44049, Columbus OH 43204. (614) 488-6176.

GERMICIDE/DISINFECTANT. According to the manufacturer, Solution II Germicide/Disinfectant is a cost-effective, nontoxic, nonirritating, double quaternary ammonium compound that is ideal for disinfecting respiratory products, requiring only a 10-minute soak with no rinsing necessary. The germicide/disinfectant comes in ready-to-use or concentrated forms, and is available in 1-ounce, 8-ounce, and 1-gallon sizes. Also available is Solution II Detergent Pre-Cleaner. Lab reports are available upon request. I.P.I. Medical Products, Dept RC, 7790 N Merrimac, Niles IL 60648. (708) 966-2200.

Authors in This Issue

Anton, William R . . . 318
Avendano, Monica A . . . 297
Avery, Mary Ellen . . . 283
Blanchette, Tim . . . 315
Buchheit, John . . . 270
Curran, John F . . . 259
Dziodzio, John . . . 315
Eid, Nemr . . . 270
Goldstein, Roger S . . . 288, 297
Gourgoulianis, KI . . . 310
Gougoulakis, ST . . . 310
Kacmarek, Robert M . . . 259
Kimmerling, Erick A . . . 267
Lain, David C . . . 319
Mathewson, Hugh S . . . 306
Melissinos, C . . . 310
Monaco, Frank . . . 315
Meredith, Keith S . . . 315
Neuling, Michelle . . . 270
Phelps, Harry . . . 270
Pierson, David J . . . 288
Smith, James K . . . 267
Stanek, Kevin S . . . 259
Stoller, James K . . . 290
Tenholder, Michael F . . . 267
Tsakraklides, V . . . 310
Weilacher, Robert R . . . 314

Advertisers in This Issue

AVL Scientific Corp . . . 250
Burroughs Wellcome Co. . . . 256a, 257, 258
CNS Inc . . . 244
ComputeR$_{X}$ Pharmacy . . . 252
FA Davis Company . . . 305
JB Lippincott Company . . . 313
MSA Catalyst Research . . . 248
HealthScan Products . . . 317
Ohmeda . . . 254
Puritan-Bennett Corp . . . Cover 2, 241
Quinton Instrument Co . . . 242
Schering Corp . . . Cover 3, Cover 4
Sherwood Medical . . . 253
Siemens Life Support Systems . . . 246

Information Requests or Change of Address

Please complete the card below

AARC Membership No. ____________

Old Address

Name ____________

Street ____________

City/State/Zip ____________

New Address

Street ____________

City/State/Zip ____________

Check the boxes below for information from the AARC

- ☐ Change of Address
- ☐ AARC Membership Info
- ☐ AARC Catalog
- ☐ AARC Position Statement

104	**AVL Scientific Corp**	Blood Gas/Hemoglobin Analyzers
118	**Burroughs Wellcome Co**	Lung Surfactant
134	**CNS Inc**	Sleep Lab and Poly G Systems
144	**FA Davis Company**	Respiratory Care Books
154	**JB Lippincott Company**	Respiratory Care Books
127	**MSA Catalyst Research**	MiniCAP 100 CO_2 Monitor
109	**HealthScan Products**	Low-Range Peak Flow Meter
110	**Ohmeda**	OxiCap 4700 Monitor
152	**Puritan-Bennett Corp**	5-Year Warranty, 7200 Series
119	**Puritan-Bennett Corp**	OmniFilter
129	**Quinton Instrument Co**	Q-Cath System
114	**Schering Corp**	Proventil Solution
139	**Sherwood Medical**	Volumetric Incentive Deep-Breathing Exerciser
124	**Siemens Life Support Systems**	Servo Ventilator
149	**ComputeR$_x$ Pharmacy**	Premixed Medicine

RESPIRATORY CARE

April Information Service **Expires July 31, 1991**

Name ____________ Ph.# ____________

Institution ____________

Address ____________

City/State/Zip ____________

Please Circle No More Than 15 Items

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140
141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160

I. Type of Instn/Practice
1. ☐ Hosp. 500 or more beds
2. ☐ Hosp. 300 to 500 beds
3. ☐ Hosp. 200 to 300 beds
4. ☐ Hosp. 100 to 200 beds
5. ☐ Hosp. 100 or less beds
6. ☐ Clinic/Group Practice
7. ☐ Independent RT Provider
8. ☐ Industry (Mfgr/Sales)

II. Department
A. ☐ Respiratory Ther.
B. ☐ Cardiopulmonary
C. ☐ Anesthesia Service
D. ☐ Emergency Dept.

III. Specialty
1. ☐ Clinical Practice
2. ☐ Perinatal Pediatrics
3. ☐ Critical Care
4. ☐ Clinical Research
5. ☐ Pulmonary Func Lab
6. ☐ Home Care/Rehab
7. ☐ Education
8. ☐ Management

IV. Position
A. ☐ Dept. Head
B. ☐ Chief Therapist
C. ☐ Supervisor
D. ☐ Staff Technician
E. ☐ Staff Therapist
F. ☐ Educator
G. ☐ Medical Director
H. ☐ Anesthesiologist
I. ☐ Other MD
J. ☐ Nurse

V. Are you a member of the AARC?
1. ☐ Yes
2. ☐ No

RESPIRATORY CARE

April Information Service Expires July 31, 1991

Name ____________ Ph.# ____________

Institution ____________

Address ____________

City/State/Zip ____________

Please Circle No More Than 15 Items

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40
41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60
61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80
81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100
101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120
121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140
141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160

I. Type of Instn/Practice
1. ☐ Hosp. 500 or more beds
2. ☐ Hosp. 300 to 500 beds
3. ☐ Hosp. 200 to 300 beds
4. ☐ Hosp. 100 to 200 beds
5. ☐ Hosp. 100 or less beds
6. ☐ Clinic/Group Practice
7. ☐ Independent RT Provider
8. ☐ Industry (Mfgr/Sales)

II. Department
A. ☐ Respiratory Ther.
B. ☐ Cardiopulmonary
C. ☐ Anesthesia Service
D. ☐ Emergency Dept.

III. Specialty
1. ☐ Clinical Practice
2. ☐ Perinatal Pediatrics
3. ☐ Critical Care
4. ☐ Clinical Research
5. ☐ Pulmonary Func Lab
6. ☐ Home Care/Rehab
7. ☐ Education
8. ☐ Management

IV. Position
A. ☐ Dept. Head
B. ☐ Chief Therapist
C. ☐ Supervisor
D. ☐ Staff Technician
E. ☐ Staff Therapist
F. ☐ Educator
G. ☐ Medical Director
H. ☐ Anesthesiologist
I. ☐ Other MD
J. ☐ Nurse

V. Are you a member of the AARC?
1. ☐ Yes
2. ☐ No

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY CARD

FIRST CLASS PERMIT NO. 2480 DALLAS, TX

POSTAGE WILL BE PAID BY ADDRESSEE

DAEDALUS ENTERPRISES INC
PO BOX 29686
DALLAS TX 75229-9691

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY CARD

FIRST CLASS PERMIT NO. 1217 BOULDER, CO

POSTAGE WILL BE PAID BY ADDRESSEE

AARC PUBLICATIONS
P.O. BOX 8758
BOULDER, CO 80328-8758

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY CARD

FIRST CLASS PERMIT NO. 1217 BOULDER, CO

POSTAGE WILL BE PAID BY ADDRESSEE

AARC PUBLICATIONS
P.O. BOX 8758
BOULDER, CO 80328-8758

Use these cards to request information from the AARC or advertisers in this issue.

IT'S THE EASY SOLUTION

Proventil®

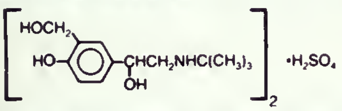
(albuterol sulfate)

Solution for Inhalation

Unit Dose 0.083%*
0.5%* 20 mL bottle

*Potency expressed as albuterol

DESCRIPTION PROVENTIL, brand of albuterol sulfate, Solution for Inhalation, is a relatively selective beta$_2$-adrenergic bronchodilator (see **CLINICAL PHARMACOLOGY** section below). Albuterol sulfate has the chemical name α^1-[(*tert*-Butylamino) methyl]-4-hydroxy-*m*-xylene-α,α'-diol sulfate (2:1) (salt), and the following chemical structure:



Albuterol sulfate has a molecular weight of 576.7 and the empirical formula $(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$. Albuterol sulfate is a white crystalline powder, soluble in water and slightly soluble in ethanol.

The international generic name for albuterol base is salbutamol.

PROVENTIL Solution for Inhalation is available in two concentrations. The 0.5% solution is in concentrated form. Dilute 0.5 mL of the solution to 3 mL with normal saline solution prior to administration. The 0.083% solution requires no dilution prior to administration.

Each mL of PROVENTIL Solution for Inhalation (0.5%) contains 5 mg of albuterol (as 6.0 mg of albuterol sulfate) in an aqueous solution containing benzalkonium chloride; sulfuric acid is used to adjust the pH between 3 and 5. PROVENTIL Solution for Inhalation (0.5%) contains no sulfiting agents. It is supplied in 20 mL bottles.

Each mL of PROVENTIL Solution for Inhalation (0.083%) contains 0.83 mg of albuterol (as 1.0 mg of albuterol sulfate) in an isotonic aqueous solution containing sodium chloride and benzalkonium chloride; sulfuric acid is used to adjust the pH between 3 and 5. PROVENTIL Solution for Inhalation (0.083%) contains no sulfiting agents. It is supplied in 3 mL bottles for unit-dose dispensing.

PROVENTIL Solution for Inhalation is a clear, colorless to light yellow solution.

CLINICAL PHARMACOLOGY The prime action of beta-adrenergic drugs is to stimulate adenyl cyclase, the enzyme which catalyzes the formation of cyclic-3',5'-adenosine monophosphate (cyclic AMP) from adenosine triphosphate (ATP). The cyclic AMP thus formed mediates the cellular responses. *In vitro* studies and *in vivo* pharmacologic studies have demonstrated that albuterol has a preferential effect on beta$_2$-adrenergic receptors compared with isoproterenol. While it is recognized that beta$_2$-adrenergic receptors are the predominant receptors in bronchial smooth muscle, recent data indicate that 10 to 50% of the beta receptors in the human heart may be beta$_2$ receptors. The precise function of these receptors, however, is not yet established. Albuterol has been shown in most controlled clinical trials to have more effect on the respiratory tract, in the form of bronchial smooth muscle relaxation, than isoproterenol at comparable doses while producing fewer cardiovascular effects. Controlled clinical studies and other clinical experience have shown that inhaled albuterol, like other beta-adrenergic agonist drugs, can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or ECG changes.

Albuterol is longer acting than isoproterenol in most patients by any route of administration because it is not a substrate for the cellular uptake processes for catecholamines nor for catechol-*O*-methyl transferase.

Studies in asthmatic patients have shown that less than 20% of a single albuterol dose was absorbed following either IPPB or nebulizer administration; the remaining amount was recovered from the nebulizer and apparatus and expired air. Most of the absorbed dose was recovered in the urine 24 hours after drug administration. Following a 3.0 mg dose of nebulized albuterol, the maximum albuterol plasma level at 0.5 hour was 2.1 ng/mL (range 1.4 to 3.2 ng/mL). There was a significant dose-related response in FEV$_1$ and peak flow rate (PFR). It has been demonstrated that following oral administration of 4 mg albuterol, the elimination half-life was 5 to 6 hours.

Animal studies show that albuterol does not pass the blood-brain barrier. Recent studies in laboratory animals (minipigs, rodents, and dogs) recorded the occurrence of cardiac arrhythmias and sudden death (with histologic evidence of myocardial necrosis) when beta-agonists and methylxanthines were administered concurrently. The significance of these findings when applied to humans is currently unknown.

In controlled clinical trials, most patients exhibited an onset of improvement in pulmonary function within 5 minutes as determined by FEV$_1$. FEV$_1$ measurements also showed that the maximum average improvement in pulmonary function usually occurred at approximately 1 hour following inhalation of 2.5 mg of albuterol by compressor-nebulizer, and remained close to peak for 2 hours. Clinically significant improvement in pulmonary function (defined as maintenance of a 15% or more increase in FEV$_1$ over baseline values) continued for 3 to 4 hours in most patients and in some patients continued up to 6 hours.

In repetitive dose studies, continued effectiveness was demonstrated throughout the 3-month period of treatment in some patients.

INDICATIONS AND USAGE PROVENTIL Solution for Inhalation is indicated for the relief of bronchospasm in patients with reversible obstructive airway disease and acute attacks of bronchospasm.

CONTRAINDICATIONS PROVENTIL Solution for Inhalation is contraindicated in patients with a history of hypersensitivity to any of its components.

WARNINGS As with other inhaled beta-adrenergic agonists, PROVENTIL Solution for Inhalation can produce paradoxical bronchospasm, which can be life threatening. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs and with the home use of sympathomimetic nebulizers. It is, therefore, essential that the physician instruct the patient in the need for further evaluation if his/her asthma becomes worse. In individual patients, any beta$_2$-adrenergic agonist, including albuterol solution for inhalation, may have a clinically significant cardiac effect.

Immediate hypersensitivity reactions may occur after administration of albuterol as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, and oropharyngeal edema.

PRECAUTIONS General: Albuterol, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias and hypertension, in patients with convulsive disorders, hyperthyroidism or diabetes mellitus, and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate preexisting diabetes mellitus and ketoacidosis. Additionally, beta-agonists, including albuterol, when given intravenously may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of PROVENTIL Solution for Inhalation is unknown.

Information For Patients: The action of PROVENTIL Solution for Inhalation may last up to 6 hours and therefore it should not be used more frequently than recommended. Do not increase the dose or frequency of medication without medical consultation. If symptoms get worse, medical consultation should be sought promptly. While taking PROVENTIL Solution for Inhalation, other anti-asthma medicines should not be used unless prescribed.

Drug Interactions: Other sympathomimetic aerosol bronchodilators or epinephrine should not be used concomitantly with albuterol.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a 2-year study in the rat, at oral doses corresponding to 10, 50, and 250 times the maximum human nebulizer dose. In another study, this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of tumorigenicity. Studies with albuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Teratogenic Effects–Pregnancy Category C: Albuterol has been shown to be teratogenic in mice when given subcutaneously in doses corresponding to the human nebulization dose. There are no adequate and well-controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice with albuterol (0.025, 0.25, and 2.5 mg/kg subcutaneously, corresponding to 0.1, 1, and 12.5 times the maximum human nebulization dose, respectively) showed cleft palate formation in 5 of 111 (4.5%) of fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) of fetuses at 2.5 mg/kg. None were observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) of fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) of fetuses at 50 mg/kg, corresponding to 250 times the maximum human nebulization dose.

Labor and Delivery: Oral albuterol has been shown to delay preterm labor in some reports. There are presently no well-controlled studies which demonstrate that it will stop preterm labor or prevent labor at term. Therefore, cautious use of PROVENTIL Solution for Inhalation is required in pregnant patients when given for relief of bronchospasm so as to avoid interference with uterine contractibility.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in some animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of albuterol solution for inhalation in children below the age of 12 years have not been established.

ADVERSE REACTIONS The results of clinical trials with PROVENTIL Solution for Inhalation in 135 patients showed the following side effects which were considered probably or possibly drug related:

Central Nervous System: tremors (20%), dizziness (7%), nervousness (4%), headache (3%), insomnia (1%).
Gastrointestinal: nausea (4%), dyspepsia (1%).
Ear, Nose and Throat: pharyngitis (<1%), nasal congestion (1%).
Cardiovascular: tachycardia (1%), hypertension (1%).
Respiratory: bronchospasm (8%), cough (4%), bronchitis (4%), wheezing (1%).

No clinically relevant laboratory abnormalities related to PROVENTIL Solution for Inhalation administration were determined in these studies.

In comparing the adverse reactions reported for patients treated with PROVENTIL Solution for Inhalation with those of patients treated with isoproterenol during clinical trials of 3 months, the following moderate to severe reactions, as judged by the investigators, were reported. This table does not include mild reactions.

Percent Incidence of Moderate To Severe Adverse Reactions

Reaction	Albuterol N = 65	Isoproterenol N = 65
Central Nervous System		
Tremors	10.7%	13.8%
Headache	3.1%	1.5%
Insomnia	3.1%	1.5%
Cardiovascular		
Hypertension	3.1%	3.1%
Arrhythmias	0%	3.0%
**Palpitation	0%	22.0%
Respiratory		
*Bronchospasm	15.4%	18%
Cough	3.1%	5%
Bronchitis	1.5%	5%
Wheeze	1.5%	1.5%
Sputum Increase	1.5%	1.5%
Dyspnea	1.5%	1.5%
Gastrointestinal		
Nausea	3.1%	0
Dyspepsia	1.5%	0
Systemic		
Malaise	1.5%	0

*In most cases of bronchospasm, this term was generally used to describe exacerbations in the underlying pulmonary disease.

**The finding of no arrhythmias and no palpitations after albuterol administration in this clinical study should not be interpreted as indicating that these adverse effects cannot occur after the administration of inhaled albuterol.

Rare cases of urticaria, angioedema, rash, bronchospasm, and oropharyngeal edema have been reported after the use of inhaled albuterol.

OVERDOSAGE Manifestations of overdosage may include anginal pain, hypertension, hypokalemia, and exaggeration of the pharmacological effects listed in **ADVERSE REACTIONS.**

The oral LD_{50} in rats and mice was greater than 2,000 mg/kg. The inhalational LD_{50} could not be determined.

There is insufficient evidence to determine if dialysis is beneficial for overdosage of PROVENTIL Solution for Inhalation.

DOSAGE AND ADMINISTRATION The usual dosage for adults and children 12 years and older is 2.5 mg of albuterol administered 3 to 4 times daily by nebulization. More frequent administration or higher doses is not recommended. To administer 2.5 mg of albuterol, either dilute 0.5 mL of the 0.5% solution for inhalation to a total volume of 3 mL with normal saline solution, or administer the contents of one unit-dose bottle (3 mL of 0.083% nebulizer solution) by nebulization. The flow rate is regulated to suit the particular nebulizer so that the PROVENTIL Solution for Inhalation will be delivered over approximately 5 to 15 minutes.

The use of PROVENTIL Solution for Inhalation can be continued as medically indicated to control recurring bouts of bronchospasm. During treatment, most patients gain optimum benefit from regular use of the nebulizer solution.

If a previously effective dosage regimen fails to provide the usual relief, medical advice should be sought immediately, as this is often a sign of seriously worsening asthma which would require reassessment of therapy.

HOW SUPPLIED PROVENTIL Solution for Inhalation, 0.5%, is a clear, colorless to light yellow solution, and is supplied in bottles of 20 mL (NDC-0085-0208-02) with accompanying calibrated dropper; boxes of one. **Store between 2° and 25°C (36° and 77°F).**

PROVENTIL Solution for Inhalation, 0.083%, is a clear, colorless to light yellow solution, and is supplied in unit-dose bottles of 3 mL each, boxes of 25 (NDC-0085-0209-01.) **Store between 2° and 25°C (36° and 77°F).**

Schering Corporation
Kenilworth, NJ 07033 USA

Revised 1/90

13934339

Copyright © 1986, 1987, 1990, Schering Corporation, Kenilworth, NJ 07033. All rights reserved.

Circle 114 on reader service card

THE *ONLY* APPROVED ALBUTEROL SULFATE UNIT DOSE

IT'S THE EASY SOLUTION

Proventil®
(albuterol sulfate)
Solution for Inhalation
Unit Dose 0.083%.*
0.5%.* 20 mL bottle
*Potency expressed as albuterol

Please see full prescribing
information on adjacent page.

Copyright © 1991, Schering Corporation.
All rights reserved.
PN-073/15290406 2/91 Printed in U.S.A.

Schering®

Schering Corporation
Kenilworth, NJ 07033